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FILE LAST UPDATED: 13 Oct 2009  (20091013/ED)
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L93       42657 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  PSEUDOMONAS AERUGINOSA
                /BI OR P. AERUGINOSA/BI
L105        624 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  ACID SPHINGOMYELINAS?/
                BI
L106         11 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L93 AND L105


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L110       1623 SEA ACID SPHINGOMYELINAS?/BI
L111         30 SEA L93 AND L110


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L112          18 DUP REM L106 L111 (23 DUPLICATES REMOVED)
                 ANSWERS '1-11' FROM FILE ZCAPLUS
                 ANSWERS '12-13' FROM FILE MEDLINE
                 ANSWER '14' FROM FILE EMBASE
                 ANSWERS '15-18' FROM FILE BIOSIS

=> d iall hitstr L112 1-11; d iall L112 12-18

L112 ANSWER 1 OF 18  ZCAPLUS  COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2009:1081806  ZCAPLUS  Full-text
ENTRY DATE:               Entered STN:  04 Sep 2009
TITLE:                    Defective acid sphingomyelinase pathway with
                          Pseudomonas aeruginosa infection in cystic fibrosis
AUTHOR(S):                Yu, Hong; Zeidan, Youssef H.; Wu, Bill X.; Jenkins,
                          Russell W.; Flotte, Terence R.; Hannun, Yusuf A.;
                          Virella-Lowell, Isabel
CORPORATE SOURCE:         Department of Pediatrics, Medical University of South
                          Carolina, Charleston, SC, USA
SOURCE:                   American Journal of Respiratory Cell and Molecular
                          Biology (2009), 41(3), 367-375
                          CODEN: AJRBEL; ISSN: 1044-1549
```

PUBLISHER: American Thoracic Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 15 (Immunochemistry)
ABSTRACT:
Acid sphingomyelinase (ASMase) is a key enzyme in sphingolipid metabolism, which can be activated by various cellular stress mechanisms including bacterial pathogens. Activation of ASMase generates ceramide, which is important for innate immune response to eliminate infected pathogens. The current study reveals a defective ASMase pathway after Pseudomonas aeruginosa infection in both a cystic fibrosis (CF) bronchial epithelial cell line (IB3-1 cell) and in the lungs of CF transmembrane conductance regulator (CFTR) knockout (KO) mice as compared with S9 cells and wild-type C57BL/6 mice. ASMase activity and total ceramide levels significantly increased in S9 cells and C57BL/6 mice with P. aeruginosa infection, but not in IB3-1 cells and CFTR KO mice. The silencing of CFTR by CFTR RNAi in S9 cells significantly decreased ASMase activity after bacterial infection as compared with controls. This study also demonstrates that induction of ASMase is responsible for modulating the immune response to bacterial infection. Blocking ASMase activity with specific ASMase RNAi, an ASMase inhibitor, or an ASMase antibody in S9 cells significantly increased IL-8 levels with P. aeruginosa infection compared with controls. Reciprocally, adding exogenous bacterial sphingomyelinase to IB3-1 cells significantly decreased IL-8 levels compared with untreated cells. In addition, silencing of ASMase in S9 cells also significantly decreased bacterial internalization. Adding exogenous bacterial sphingomyelinase to IB3-1 cells reconstituted the cell death response to P. aeruginosa infection. This study demonstrates that the defective ASMase pathway in CF is a key contributor to the unabated IL-8 response with P. aeruginosa infection and to the compromised host response failing to eradicate bacteria.

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L112 ANSWER 2 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2009:829732 ZCAPLUS Full-text
ENTRY DATE: Entered STN: 10 Jul 2009
TITLE: Therapeutic Efficacy and Safety of Amitriptyline in Patients with Cystic Fibrosis
AUTHOR(S): Riethmueller, Joachim; Anthonysamy, Janina; Serra, Emilio; Schwab, Matthias; Doering, Gerd; Gulbins, Erich
CORPORATE SOURCE: Department of Paediatrics, University Hospital Tuebingen, Tuebingen, D-72076, Germany
SOURCE: Cellular Physiology and Biochemistry (2009), 24(1-2), 65-72
CODEN: CEPBEW; ISSN: 1015-8987
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1 (Pharmacology)
ABSTRACT:
Amitriptyline, a blocker of acid sphingomyelinase and acid ceramidase, significantly reduces Pseudomonas aeruginosa lung infection in cystic

fibrosis (CF) mice with concurrent increase of survival. Our aim was to establish whether amitriptyline is safe and effective in the treatment of CF patients. In a randomised, double-blinded, placebo-controlled, cross-over pilot study, 4 adult CF patients received 37.5 mg of amitriptyline or placebo twice daily for 14 days. Subsequently in a phase II study 19 adult CF patients were randomly allocated to three treatment groups receiving amitriptyline once daily for 28 days at doses of 25 mg (n=7), 50 mg (n=8), or 75 mg (n=8) or placebo (n=13). The primary outcome was the difference of forced expiratory volume in 1 s (FEV1) at day 14 between amitriptyline and placebo. Primary endpoint measures improved significantly in three of four patients in the pilot study after amitriptyline treatment vs placebo (relative FEV1: 14.7±5%; p = 0.006) and in the 25 mg treatment group of the phase II study (relative FEV1: 4.0±7%; p = 0.048). Amitriptyline was well tolerated in both studies and 96% of the patients completed the studies. Amitriptyline as a novel therapeutic option in patients with CF is safe and seems to be efficacious.

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L112 ANSWER 3 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2008:1064754 ZCAPLUS Full-text
DOCUMENT NUMBER: 149:511238
ENTRY DATE: Entered STN: 04 Sep 2008
TITLE: Acid Sphingomyelinase Amplifies Redox Signaling in Pseudomonas aeruginosa-Induced Macrophage Apoptosis
AUTHOR(S): Zhang, Yang; Li, Xiang; Carpinteiro, Alexander; Gulbins, Erich
CORPORATE SOURCE: Institute of Molecular Biology, University of Duisburg-Essen, Essen, 45122, Germany
SOURCE: Journal of Immunology (2008), 181(6), 4247-4254
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 15-8 (Immunochemistry)
ABSTRACT:
Recent studies indicate that distinct membrane microdomains, also named lipid rafts, and ceramide play an important role in infectious biol. Ceramide forms larger ceramide-enriched membrane platforms that are required for diverse

signal transduction. Here, the authors demonstrate that ceramide-enriched membrane platforms are critically involved in redox signaling that regulates alveolar macrophage apoptosis upon infection with P. aeruginosa. In freshly isolated alveolar macrophages, P. aeruginosa infection results in rapid activation of acid sphingomyelinase (Asm), release of ceramide, and formation of ceramide-enriched membrane platforms, which are required for P. aeruginosa-induced activation of NADPH oxidase and production of reactive oxygen species (ROS). Inhibition of NADPH oxidase or removal of intracellular ROS reduced P. aeruginosa-induced activation of the Asm and formation of ceramide-enriched membrane platforms, suggesting that NADPH oxidase-derived ROS regulate Asm-initiated redox signaling in a pos. feedback manner. Furthermore, stimulation of JNK and induction of apoptosis upon P. aeruginosa infections are dependent on NADPH oxidase-derived ROS. Thus, ceramide-enriched membrane platforms are essential for amplification of Asm-mediated redox signaling, which mediates JNK activation and thereby apoptosis of alveolar macrophages upon P. aeruginosa infection.

SUPPL. TERM: acid sphingomyelinase redox signaling Pseudomonas infection macrophage apoptosis

INDEX TERM: Macrophage
(alveolar; ceramide-enriched membrane platforms are essential for amplification of acid sphingomyelinase-mediated redox signaling which mediated JNK activation in Pseudomonas aeruginosa infection-induced macrophage apoptosis)

INDEX TERM: Apoptosis
Lipid raft
Macrophage
Pseudomonas aeruginosa
Redox reaction
Signal transduction
(ceramide-enriched membrane platforms are essential for amplification of acid sphingomyelinase -mediated redox signaling which mediated JNK activation in Pseudomonas aeruginosa infection-induced macrophage apoptosis)

INDEX TERM: Ceramides
Reactive oxygen species
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide-enriched membrane platforms are essential for amplification of acid sphingomyelinase -mediated redox signaling which mediated JNK activation in Pseudomonas aeruginosa infection-induced macrophage apoptosis)

INDEX TERM: Lung
(macrophage; ceramide-enriched membrane platforms are essential for amplification of acid sphingomyelinase-mediated redox signaling which mediated JNK activation in Pseudomonas aeruginosa infection-induced macrophage apoptosis)

INDEX TERM: 7782-44-7D, Oxygen, reactive species, biological studies
9031-54-3, Sphingomyelinase C 9032-22-8, NADPH oxidase
155215-87-5, JNK kinase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide-enriched membrane platforms are essential for amplification of acid sphingomyelinase

-mediated redox signaling which mediated JNK activation in Pseudomonas aeruginosa infection-induced macrophage apoptosis)
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 16 Sep 2009
OS.CITING.REFS: CAPLUS 2009:1079259; 2009:376758
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD.
REFERENCE(S):
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L112 ANSWER 4 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2008:1343334 ZCAPLUS Full-text
DOCUMENT NUMBER: 150:18250
ENTRY DATE: Entered STN: 07 Nov 2008
TITLE: Ceramide in bacterial infections and cystic fibrosis
AUTHOR(S): Grassme, Heike; Becker, Katrin Anne; Zhang, Yang; Gulbins, Erich
CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Essen, D-45122, Germany
SOURCE: Biological Chemistry (2008), 389(11), 1371-1379 CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: Walter de Gruyter GmbH & Co. KG

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
CLASSIFICATION: 14-0 (Mammalian Pathological Biochemistry)
ABSTRACT:
A review. Ceramide is formed by the activity of sphingomyelinases, by degradation of complex sphingolipids, reverse ceramidase activity or de novo synthesized. The formation of ceramide within biol. membranes results in the formation of large ceramide-enriched membrane domains. These domains serve the spatial and temporal organization of receptors and signaling mols. The acid sphingomyelinase-ceramide system plays an important role in the infection of mammalian host cells with bacterial pathogens such as Neisseria gonorrhoeae, Escherichia coli, Staphylococcus aureus, Listeria monocytogenes, Salmonella typhimurium and Pseudomonas aeruginosa. Ceramide and ceramide-enriched membrane platforms are also involved in the induction of apoptosis in infected cells, such as in epithelial and endothelial cells after infection with Pseudomonas aeruginosa and Staphylococcus aureus, resp. Finally, ceramide-enriched membrane platforms are critical regulators of the release of pro-inflammatory cytokines upon infection. The diverse functions of ceramide in bacterial infections suggest that ceramide and ceramide-enriched membrane domains are key players in host responses to many pathogens and thus are potential novel targets to treat infections.

SUPPL. TERM: review ceramide infection bacteria cystic fibrosis
INDEX TERM: Bacterial infection
Cell membrane
Cystic fibrosis
Escherichia coli
Human
Listeria monocytogenes
Mycobacterium
Neisseria gonorrhoeae
Pseudomonas aeruginosa
Salmonella typhimurium
Staphylococcus aureus
(ceramide in bacterial infections and cystic fibrosis)
INDEX TERM: Ceramides
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide in bacterial infections and cystic fibrosis)
INDEX TERM: 9031-54-3, Sphingomyelinase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide in bacterial infections and cystic fibrosis)
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 23 Apr 2009
OS.CITING.REFS: CAPLUS 2009:446361; 2008:1343331
REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD.
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L112 ANSWER 5 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2008:439128 ZCAPLUS Full-text
DOCUMENT NUMBER: 149:6518
ENTRY DATE: Entered STN: 09 Apr 2008
TITLE: Ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis
AUTHOR(S): Teichgraeber, Volker; Ulrich, Martina; Endlich, Nicole; Riethmueller, Joachim; Wilker, Barbara; De Oliveira-Munding, Cheyla Conceicao; van Heeckeren, Anna M.; Barr, Mark L.; von Kuerthy, Gabriele; Schmid, Kurt W.; Weller, Michael; Tuemmler, Burkhard; Lang, Florian; Grassme, Heike; Doering, Gerd; Gulbins, Erich
CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Essen, 45122, Germany
SOURCE: Nature Medicine (New York, NY, United States) (2008), 14(4), 382-391
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 14-4 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1

ABSTRACT:
Microbial lung infections are the major cause of morbidity and mortality in the hereditary metabolic disorder cystic fibrosis, yet the mol. mechanisms leading from the mutation of cystic fibrosis transmembrane conductance regulator (CFTR) to lung infection are still unclear. Here, we show that ceramide age-dependently accumulates in the respiratory tract of uninfected Cftr-deficient mice owing to an alkalinization of intracellular vesicles in Cftr-deficient cells. This change in pH results in an imbalance between acid

sphingomyelinase (Asm) cleavage of sphingomyelin to ceramide and acid ceramidase consumption of ceramide, resulting in the higher levels of ceramide. The accumulation of ceramide causes Cftr-deficient mice to suffer from constitutive age-dependent pulmonary inflammation, death of respiratory epithelial cells, deposits of DNA in bronchi and high susceptibility to severe Pseudomonas aeruginosa infections. Partial genetic deficiency of Asm in Cftr-/-Smpd1+/- mice or pharmacol. treatment of Cftr-deficient mice with the Asm blocker amitriptyline normalizes pulmonary ceramide and prevents all pathol. findings, including susceptibility to infection. These data suggest inhibition of Asm as a new treatment strategy for cystic fibrosis.

SUPPL. TERM: ceramide inflammation infection susceptibility cystic fibrosis

INDEX TERM: Cystic fibrosis
Human
Pneumonitis
Pseudomonas aeruginosa
Respiratory system
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: CFTR (cystic fibrosis transmembrane conductance regulator)
Ceramides
ROLE: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: Sphingomyelins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: DNA
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(deposits in respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: Respiratory system
(epithelium, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: Apoptosis
(of respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: Epithelium
(respiratory tract, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: Organelle
(vesicle, alkalinization of; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: 57-88-5, Cholesterol, biological studies 123-78-4, Sphingosine 9031-54-3, Acid sphingomyelinase 26993-30-6, Sphingosine 1-phosphate 37289-06-8, Acid ceramidase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide accumulation mediates inflammation, cell death

and infection susceptibility in cystic fibrosis)

INDEX TERM: 212059-03-5, Peptamen
ROLE: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

INDEX TERM: 50-48-6, Amitriptyline
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

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L112 ANSWER 6 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2007:1284150 ZCAPLUS Full-text
DOCUMENT NUMBER: 148:50999
ENTRY DATE: Entered STN: 12 Nov 2007
TITLE: Ceramide in Pseudomonas aeruginosa infections
AUTHOR(S): Riethmueller, Joachim; Riehle, Andrea; Grassme, Heike; Gulbins, Erich
CORPORATE SOURCE: Children's Hospital, University of Tuebingen, Tuebingen, Germany
SOURCE: European Journal of Lipid Science and Technology (2007), 109(10), 998-1002
CODEN: EJLTFM; ISSN: 1438-7697
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
CLASSIFICATION: 14-0 (Mammalian Pathological Biochemistry)

ABSTRACT:
A review. Cystic fibrosis (CF), the most common autosomal recessive disorder, at least in western countries, is caused by mutations of the cystic fibrosis transmembranous conductance regulator (CFTR) mol. and affects approx. 80,000 patients in Europe and the USA. Most, if not all, CF patients develop a chronic pulmonary infection with Pseudomonas aeruginosa. At present it is unknown why CF patients are highly sensitive to P. aeruginosa infections, and most importantly, no curative treatment for CF is available. P. aeruginosa infection results in an activation of the enzyme acid sphingomyelinase which catalyzes the release of ceramide from sphingomyelin in the cell membrane. Ceramide forms large ceramide-enriched membrane domains that are required for internalization of bacteria, induction of cell death in infected cells and a controlled release of cytokines from infected cells. Ceramide-enriched membrane platforms seem to serve the reorganization of receptors and intracellular signaling mols. involved in the infection of mammalian cells with P. aeruginosa. The significance of the acid sphingomyelinase and ceramide for the infection of mammalian cells with P. aeruginosa was demonstrated on mice genetically deficient for the acid sphingomyelinase. Further studies with N. gonorrhoeae, S. aureus and rhinoviruses indicate that ceramide-enriched membrane domains are also important for the infection of mammalian cells with other bacterial and viral pathogens, suggesting a general role of these membrane domains in infectious biol.

SUPPL. TERM: review ceramide membrane bacteria infection internalization; Pseudomonas infection internalization ceramide membrane review
INDEX TERM: Bacterial infection
Cell membrane

Human
Pseudomonas aeruginosa
(ceramide-enriched membrane domains in bacterial infections)

INDEX TERM: Ceramides
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide-enriched membrane domains in bacterial infections)

INDEX TERM: Biological transport
(internalization; ceramide-enriched membrane domains in bacterial infections)

INDEX TERM: 9031-54-3, Acid sphingomyelinase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide-enriched membrane domains in bacterial infections)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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L112 ANSWER 7 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 8

ACCESSION NUMBER:	2005:598564 ZCAPLUS Full-text
DOCUMENT NUMBER:	143:130905
ENTRY DATE:	Entered STN: 11 Jul 2005
TITLE:	Rhinoviruses Infect Human Epithelial Cells via Ceramide-enriched Membrane Platforms
AUTHOR(S):	Grassme, Heike; Riehle, Andrea; Wilker, Barbara; Gulbins, Erich
CORPORATE SOURCE:	Department of Molecular Biology, University of Duisburg-Essen, Essen, 45122, Germany
SOURCE:	Journal of Biological Chemistry (2005), 280(28), 26256-26262 CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER:	American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE:	Journal
LANGUAGE:	English
CLASSIFICATION:	14-3 (Mammalian Pathological Biochemistry) Section cross-reference(s): 10

ABSTRACT:
The cell membrane contains very small distinct membrane domains enriched of sphingomyelin and cholesterol that are named rafts. We have shown that the formation of ceramide via activation of the acid sphingomyelinase transforms rafts into ceramide-enriched membrane platforms. These platforms are required for infection of mammalian cells with Pseudomonas aeruginosa, Staphylococcus aureus, or Neisseriae gonorrhoeae. In the present study we determined whether the acid sphingomyelinase, ceramide, and ceramide-enriched membrane platforms are also involved in the infection of human cells with pathogenic rhinoviruses. We demonstrate that infection of human epithelial cells with several rhinovirus strains triggers a rapid activation of the acid sphingomyelinase correlating with microtubules- and microfilament-mediated

translocation of the enzyme from an intracellular compartment onto the extracellular leaflet of the cell membrane. The activity of the acid sphingomyelinase results in the formation of ceramide in the cell membrane and, finally, large ceramide-enriched membrane platforms. Rhinoviruses colocalize with ceramide-enriched membrane platforms during the infection. The significance of ceramide-enriched membrane platforms for rhino-viral uptake is demonstrated by the finding that genetic deficiency or pharmacol. inhibition of the acid sphingomyelinase prevented infection of human epithelial cells by rhinoviruses. The data identify the acid sphingomyelinase and ceramide as key mols. for the infection of human cells with rhinoviruses.

SUPPL. TERM: Rhinovirus infection human epithelium via ceramide enriched membrane platform
INDEX TERM: Ceramides
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(-enriched membrane platforms; Rhinoviruses infect human epithelial cells via ceramide-enriched membrane platforms)
INDEX TERM: Cell membrane
Epithelium
Human
(Rhinoviruses infect human epithelial cells via ceramide-enriched membrane platforms)
INDEX TERM: Enzymes, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(epithelium infection with rhinovirus triggers acid sphingomyelinase activation and enzyme translocation from an intracellular compartment onto extracellular leaflet of cell membrane)
INDEX TERM: Rhinovirus
(infection with; Rhinoviruses infect human epithelial cells via ceramide-enriched membrane platforms)
INDEX TERM: Biological transport
(intracellular, of enzyme; epithelium infection with rhinovirus triggers acid sphingomyelinase activation and enzyme translocation from an intracellular compartment onto extracellular leaflet of cell membrane)
INDEX TERM: 9031-54-3, Acid sphingomyelinase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(epithelium infection with rhinovirus triggers acid sphingomyelinase activation and enzyme translocation from an intracellular compartment onto extracellular leaflet of cell membrane)
OS.CITING REF COUNT: 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS RECORD (44 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 12 Oct 2009
OS.CITING.REFS: CAPLUS 2009:1032914; 2009:1006262; 2009:996182; 2009:589754; 2009:376758; 2009:372312; 2009:386656; 2009:44159; 2009:44158; 2009:58346; 2008:1452977; 2008:1343334; 2008:1309078; 2008:1264338; 2008:1209070; 2008:1040833; 2008:591706; 2008:569088; 2008:302972; 2008:250538; 2008:89744; 2007:1284150; 2007:1235734; 2007:1043948; 2007:1043947; 2007:859178; 2007:830517; 2007:712504; 2007:668836; 2007:628302; 2007:585881; 2007:565841; 2007:221740; 2007:114381; 2007:40331; 2007:15526; 2006:1297535; 2006:1262839; 2006:747507;

2006:552307; 2006:242769; 2006:64884; 2005:1349655; 2005:1349649

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L112 ANSWER 8 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 2005:1349655 ZCAPLUS Full-text
DOCUMENT NUMBER: 144:86223
ENTRY DATE: Entered STN: 29 Dec 2005
TITLE: Ceramide-enriched membrane domains
AUTHOR(S): Bollinger, Claudia R.; Teichgraeber, Volker; Gulbins, Erich
CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Essen, 45122, Germany
SOURCE: Biochimica et Biophysica Acta, Molecular Cell Research (2005), 1746(3), 284-294
CODEN: BBAMCO; ISSN: 0167-4889
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
CLASSIFICATION: 15-0 (Immunochemistry)
ABSTRACT:

A review. Cellular activation involves the re-organization of receptor mols. and the intracellular signalosome in the cell membrane. Recent studies indicate that specialized domains of the cell membrane, termed rafts, are central for the spatial organization of receptors and signaling mols. Rafts are converted into larger membrane platforms by activity of the acid sphingomyelinase, which hydrolyzes raft-sphingomyelin to ceramide. Ceramide mols. spontaneously associate to form ceramide-enriched microdomains, which fuse to large ceramide-enriched membrane platforms. The acid sphingomyelinase is activated by multiple stimuli including CD95, CD40, DR5/TRAIL, CD20, FcγRII, CD5, LFA-1, CD28, TNF, the Interleukin-1 receptor, the PAF-receptor, CD14, infection with P. aeruginosa, S. aureus, N. gonorrhoeae, Sindbis-Virus, Rhinovirus, treatment with γ-irradiation, UV-light, doxorubicin, cisplatin, disruption of integrin-signaling and under some conditions of developmental death. Ceramide-enriched membrane platforms serve the clustering of receptors, the recruitment of intracellular signaling mols. and the exclusion of inhibitory signaling factors and, thus, facilitate signal transduction initiated by the specific stimulus.

SUPPL. TERM: review ceramide membrane domain signaling
INDEX TERM: Cell membrane
Protein motifs
Signal transduction, biological
(ceramide-enriched membrane domains)
INDEX TERM: Ceramides
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide-enriched membrane domains)
OS.CITING REF COUNT: 84 THERE ARE 84 CAPLUS RECORDS THAT CITE THIS RECORD (84 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 07 Oct 2009
OS.CITING.REFS: CAPLUS 2009:1081806; 2009:1006262; 2009:996182; 2009:988562; 2009:959810; 2009:783662; 2009:604070; 2009:704096; 2009:247338; 2009:571938; 2009:725310; 2009:720247; 2009:478101; 2009:308170; 2009:337282; 2009:254929; 2009:464332; 2009:337123; 2009:14418; 2009:44165; 2009:44164; 2009:44158; 2009:60223; 2008:1517639; 2008:1361955; 2008:1319638; 2008:1285826; 2008:1256082; 2008:1253733; 2008:1086581; 2008:1072029; 2008:1025590; 2008:1008697; 2008:745538; 2008:728037; 2008:620317; 2008:557847; 2008:405843; 2008:323697; 2008:304136; 2008:302972; 2008:250538; 2008:227631; 2008:175879; 2008:134198; 2008:93518; 2008:89745; 2008:58739; 2008:47089; 2007:1390830
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L112 ANSWER 9 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 2003:155313 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:270184
ENTRY DATE: Entered STN: 28 Feb 2003
TITLE: Host defense against Pseudomonas aeruginosa requires ceramide-rich membrane rafts
AUTHOR(S): Grassme, H.; Jendrossek, V.; Riehle, A.; von Kuerthy, G.; Berger, J.; Schwarz, H.; Weller, M.; Kolesnick, R.; Gulbins, E.
CORPORATE SOURCE: Department of Molecular Biology, University of Essen, Essen, Germany
SOURCE: Nature Medicine (New York, NY, United States) (2003), 9(3), 322-330
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 15-8 (Immunochemistry)
Section cross-reference(s): 10

ABSTRACT:
Pseudomonas aeruginosa infection is a serious complication in patients with cystic fibrosis and in immunocompromised individuals. Here the authors show that P. aeruginosa infection triggers activation of the acid sphingomyelinase and the release of ceramide in sphingolipid-rich rafts. Ceramide reorganizes these rafts into larger signaling platforms that are required to internalize P. aeruginosa, induce apoptosis and regulate the cytokine response in infected cells. Failure to generate ceramide-enriched membrane platforms in infected cells results in an unabated inflammatory response, massive release of interleukin (IL)-1 and septic death of mice. These findings show that ceramide-enriched membrane platforms are central to the host defense against this potentially lethal pathogen.

SUPPL. TERM: Pseudomonas infection ceramide membrane raft
INDEX TERM: Infection
(bacterial; release in tracheal epithelium by Pseudomonas aeruginosa is required for membrane raft-dependent infection)
INDEX TERM: Fas antigen
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(clustering in human nasal tracheal epithelium by Pseudomonas aeruginosa infection)
INDEX TERM: CFTR (cystic fibrosis transmembrane conductance regulator)
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(clustering in mouse tracheal epithelium by Pseudomonas aeruginosa infection)
INDEX TERM: Nose
Trachea (anatomical)
(epithelium, infection; release in tracheal epithelium by Pseudomonas aeruginosa is required for membrane raft-dependent infection)
INDEX TERM: Pseudomonas aeruginosa
(host defense against Pseudomonas

aeruginosa requires ceramide-rich membrane rafts)
INDEX TERM: Cystic fibrosis
(host defense against Pseudomonas aeruginosa requires ceramide-rich membrane rafts in relation to)
INDEX TERM: Cell membrane
(lipid raft; release in tracheal epithelium by Pseudomonas aeruginosa is required for membrane raft-dependent infection)
INDEX TERM: Epithelium
(nasal, infection; release in tracheal epithelium by Pseudomonas aeruginosa is required for membrane raft-dependent infection)
INDEX TERM: Apoptosis
(of airway epithelial cells by Pseudomonas aeruginosa is prevented by blockade of sphingolipid-enriched rafts)
INDEX TERM: Interleukin 1β
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(release by nasal epithelium is sphingolipid-enriched raft-dependent in Pseudomonas aeruginosa infection)
INDEX TERM: Human
(release in tracheal epithelium by Pseudomonas aeruginosa is required for membrane raft-dependent infection)
INDEX TERM: Ceramides
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(release in tracheal epithelium by Pseudomonas aeruginosa is required for membrane raft-dependent infection)
INDEX TERM: Epithelium
(tracheal, infection; release in tracheal epithelium by Pseudomonas aeruginosa is required for membrane raft-dependent infection)
INDEX TERM: 9031-54-3, Acid sphingomyelinase
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(activation in tracheal epithelium by Pseudomonas aeruginosa is required for ceramide-dependent infection)
OS.CITING REF COUNT: 147 THERE ARE 147 CAPLUS RECORDS THAT CITE THIS RECORD (147 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 07 Oct 2009
OS.CITING.REFS: CAPLUS 2009:1081806; 2009:1081800; 2009:1006262; 2009:829732; 2009:799592; 2009:1022350; 2009:589754; 2009:535182; 2008:878329; 2009:338512; 2009:254928; 2009:130629; 2009:396826; 2009:44159; 2009:217418; 2009:58346; 2008:1496580; 2009:173669; 2008:1343334; 2008:1322821; 2008:1319638; 2008:1256082; 2008:1229802; 2008:1223872; 2008:1209070; 2008:1064754; 2008:1064698; 2008:962169; 2008:745538; 2008:579460; 2008:569088; 2008:487313; 2008:453631; 2008:439128; 2008:439110; 2008:414006; 2008:340125; 2008:302972; 2008:250538; 2008:164892; 2008:140294; 2008:121997; 2008:93518; 2008:40360; 2008:14379; 2007:1284150; 2007:1284145; 2007:1248650; 2007:1235734; 2007:1216982
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L112 ANSWER 10 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:766319 ZCAPLUS Full-text

DOCUMENT NUMBER: 149:143664

ENTRY DATE: Entered STN: 26 Jun 2008

TITLE: Improved pulmonary function by acid sphingomyelinase inhibition in a newborn piglet lavage model

AUTHOR(S): von Bismarck, Philipp; Wistaedt, Carlos-Francisco Garcia; Klemm, Karsten; Winoto-Morbach, Supandi; Uhlig, Ulrike; Schuetze, Stefan; Adam, Dieter; Lachmann, Burkhard; Uhlig, Stefan; Krause, Martin F.

CORPORATE SOURCE: Department of Pediatrics, Universitaetsklinikum Schleswig-Holstein, Kiel, Germany

SOURCE: American Journal of Respiratory and Critical Care Medicine (2008), 177(11), 1233-1241
CODEN: AJCMED; ISSN: 1073-449X

PUBLISHER: American Thoracic Society

DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 1-9 (Pharmacology)

ABSTRACT:
Rationale: In acute inflammatory lung disease in newborn infants, exogenous surfactant only transiently improves lung function. We hypothesized that the transient nature of this protection is in part explained by elevated acid sphingomyelinase (a-SMase) activity that may inactivate surfactant and promote proinflammatory responses. Objectives: We investigated the intermediate-term effects (>12h) of a-SMase inhibition in a neonatal piglet model of repeated airway lavage by the intratracheal use of the a-SMase inhibitor imipramine, together with exogenous surfactant as a carrier substance. Methods: After surfactant washout and induction of pulmonary inflammation, lung function was monitored over 24 h of mech. ventilation and followed by ex vivo analyses. In addition, we studied the effect of lipopolysaccharide inhalation in a-SMase-deficient mice at 48 h. Measurements and Main Results: Surfactant washout increased both pulmonary a-SMase activity and ceramide content; this was attenuated by surfactant and prevented in the surfactant plus imipramine group. Compared with surfactant alone, PaO2, dynamic compliance, and extravascular lung water were improved in the final 12 h in the surfactant plus imipramine group. At 24 h, lavage fluid leukocyte counts and IL-8 concns. decreased, and phys. surfactant film properties improved. In the mouse model at 48 h, a-SMase-deficient mice showed reduced pulmonary ceramide levels and attenuated leukocyte influx into the alveolar space. Conclusions: We conclude that stabilization of exogenous surfactant by adding imipramine to create a "fortified surfactant preparation" improves lung function in a clin. relevant piglet model, and that this effect can be attributed to the inhibition of a-SMase as evidenced in the mouse model.

SUPPL. TERM: imipramine surfactant airway lavage neonate
INDEX TERM: Transcription factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-κB (nuclear factor of κ light chain gene enhancer in B-cells); surfactant alone or in combination with imipramine reduced nuclear factor κB translocation to nucleus of pulmonary cell in neonatal piglet model of repeated airway lavage)
INDEX TERM: Leukocyte
(imipramine and surfactant decreased polymorphonuclear leukocyte count in neonatal piglet model of repeated airway lavage)
INDEX TERM: Ceramides
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(imipramine and surfactant inhibited ceramide level in neonatal piglet model of repeated airway lavage)
INDEX TERM: Lung
Newborn
Pulmonary surfactant
(imipramine and surfactant inhibited sphingomyelinase activity, ceramide level and was improved lung function in neonatal piglet model of repeated airway lavage)
INDEX TERM: Pulmonary edema
(imipramine and surfactant inhibited sphingomyelinase activity, reduced pulmonary edema, ceramide level and was improved lung function in neonatal piglet model of repeated airway lavage)
INDEX TERM: Breathing (animal)
(imipramine and surfactant stabilized ventilation

efficacy in neonatal piglet model of repeated airway lavage)

INDEX TERM: Pneumonitis
(sphingomyelinase was involved in antiinflammatory activity of imipramine in mouse model of inflammatory lung injury induced by Pseudomonas aeruginosa lipopolysaccharide inhalation)

INDEX TERM: Interleukin 8
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(surfactant alone or in combination with imipramine reduced interleukin 8 level in neonatal piglet model of repeated airway lavage)

INDEX TERM: Surface tension
(surfactant alone or in combination with imipramine reduced surface tension in neonatal piglet model of repeated airway lavage)

INDEX TERM: 124-38-9, Carbon dioxide, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(imipramine and surfactant did not alter partial pressure of carbon dioxide in neonatal piglet model of repeated airway lavage)

INDEX TERM: 7782-44-7, Oxygen, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(imipramine and surfactant did not alter partial pressure of oxygen in neonatal piglet model of repeated airway lavage)

INDEX TERM: 9031-54-3, Sphingomyelinase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(imipramine and surfactant inhibited sphingomyelinase activity in neonatal piglet model of repeated airway lavage)

INDEX TERM: 50-49-7, Imipramine
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imipramine and surfactant inhibited sphingomyelinase activity, ceramide level and was improved lung function in neonatal piglet model of repeated airway lavage)

INDEX TERM: 71160-24-2, Leukotriene B4
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(surfactant alone or in combination with imipramine reduced leukotriene B4 level in neonatal piglet model of repeated airway lavage)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

DATE LAST CITED: Date last citing reference entered STN: 02 Mar 2009

OS.CITING.REFS: CAPLUS 2009:58346; 2008:1209070

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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L112 ANSWER 11 OF 18 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1380149 ZCAPLUS Full-text
ENTRY DATE: Entered STN: 18 Nov 2008
TITLE: Ceramide accumulation mediates inflammation, cell death, and infection susceptibility in cystic fibrosis
AUTHOR(S): Teichgraber, V.; Ulrich, M.; Endlich, N.
SOURCE: Chemtracts (2007), 20(10), 434-436
CODEN: CHEMFW; ISSN: 1431-9268
PUBLISHER: Data Trace Publishing Co.
DOCUMENT TYPE: Journal; Miscellaneous
LANGUAGE: English

ABSTRACT:
Cystic fibrosis is a genetic disorder that causes a progressive accumulation of mucus in lungs and other tissues of affected individuals. It is caused by a mutation in the cystic fibrosis trans-membrane conductance regulator (CFTR) gene that results in impairments of the ion channel important in the production of mucus, sweat, and gastric juices. It has been observed that individuals with cystic fibrosis are prone to bacterial infection and this study aimed to determine the cause of this microbial susceptibility. Teichgraber and coworkers also looked at alterations in the metabolism and role of sphingolipids in cystic fibrosis. Using CFTR-deficient mice, the investigators showed that ceramide accumulated in an age-dependent manner in the lungs of the mutant mice. Accumulation was observed in the respiratory tract epithelium and submucosal glands which was similarly observed in adult individuals with cystic fibrosis. Further studies showed that CFTR deficiency leads to a pH shift from 4.5 to 5.9, which results in an imbalance in the activity of acid sphingomyelinase and ceramidase. In fact, acid ceramidase reversed its activity, causing production of ceramide rather than degrading it. Thus, alkalinization results only in slight reduction of the activity of Asm, the enzyme producing ceramide, while inhibiting breakdown of ceramide by ceramidase, which at pH 5.9 reverses its activity, thereby producing more ceramide that accumulates in respiratory epithelial cells. Ceramide accumulation is blocked in pulmonary vesicles when these were acidified. The increase in ceramide concentration in the lungs at pH 5.9
led to increased cytokine production causing inflammation, increased respiratory epithelial cell death, and deposition of DNA that made the cells susceptible to Pseudomonas aeruginosa infection. Knock-out of Asm in mice as well as inhibition studies on Asm using amitriptyline also resulted in reduction of ceramide accumulation in the cells, suggesting that inhibition of ceramide accumulation may be a new approach for ameliorating the effects of cystic fibrosis.

L112 ANSWER 12 OF 18 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2004274053 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15069600
TITLE: Ceramide, membrane rafts and infections.
AUTHOR: Gulbins Erich; Dreschers Stephan; Wilker Barbara; Grassme Heike
CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany.. erich.gulbins@uni-essen.de
SOURCE: Journal of molecular medicine (Berlin, Germany), (2004 Jun) Vol. 82, No. 6, pp. 357-63. Electronic Publication: 2004-04-07. Ref: 42
Journal code: 9504370. ISSN: 0946-2716.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 3 Jun 2004
Last Updated on STN: 30 Oct 2004
Entered Medline: 29 Oct 2004
ABSTRACT:
Distinct domains in the cell membrane, termed rafts, emerge as central for the

infection of mammalian cells by many pathogens. Rafts consist of sphingolipids and cholesterol that interact strongly, and thus spontaneously separate from other phospholipids in the cell membrane. Recent studies suggest that at least some pathogens activate the acid sphingomyelinase that releases ceramide in membrane rafts. The generation of ceramide transforms small rafts into a signaling unit and results in the fusion of small rafts to large platforms. Membrane rafts and ceramide-enriched membrane platforms have been shown to mediate internalization of bacteria, viruses and parasites into the host cell, to initiate apoptosis of the host cell upon infection and to regulate the release of cytokines from infected mammalian cells. Furthermore, rafts and ceramide have been implicated in the intracellular trafficking of phagosomes and in the budding of viruses from infected cells. The molecular function of rafts and ceramide-enriched membrane platforms seems to be the re-organization of receptor and intracellular signaling molecules in the cell membrane permitting the interaction of the pathogen with the cell. This suggests that rafts and ceramide-enriched membrane platforms function as central structures involved in the infection of mammalian cells by pathogens and as targets for the development of anti-infective drugs.

CONTROLLED TERM: Animals
Apoptosis
Ceramides: IM, immunology
*Ceramides: PH, physiology
Cytokines: BI, biosynthesis
Humans
*Infection: PP, physiopathology
Membrane Microdomains: MI, microbiology
*Membrane Microdomains: PH, physiology
Phagosomes: PH, physiology
Pseudomonas Infections: PP, physiopathology
Pseudomonas aeruginosa: PY, pathogenicity
*Signal Transduction

CHEMICAL NAME: 0 (Ceramides); 0 (Cytokines)

L112 ANSWER 13 OF 18 MEDLINE on STN

ACCESSION NUMBER: 2009476152 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 19590194

TITLE: Therapeutic efficacy and safety of amitriptyline in patients with cystic fibrosis.

AUTHOR: Riethmuller Joachim; Anthonysamy Janina; Serra Emilio; Schwab Matthias; Doring Gerd; Gulbins Erich

CORPORATE SOURCE: Department of Paediatrics, University Hospital Tuebingen, Tuebingen, Germany..
joachim.riethmueller@med.uni-tuebingen.de

SOURCE: Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology, (2009) Vol. 24, No. 1-2, pp. 65-72.
Electronic Publication: 2009-07-01.
Journal code: 9113221. E-ISSN: 1421-9778.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: (CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(CLINICAL TRIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200910

ENTRY DATE: Entered STN: 11 Jul 2009
Last Updated on STN: 6 Oct 2009

Entered Medline: 5 Oct 2009

ABSTRACT:
Amitriptyline, a blocker of acid sphingomyelinase and acid ceramidase, significantly reduces Pseudomonas aeruginosa lung infection in cystic fibrosis (CF) mice with concurrent increase of survival. Our aim was to establish whether amitriptyline is safe and effective in the treatment of CF patients. In a randomised, double-blinded, placebo-controlled, cross-over pilot study, 4 adult CF patients received 37.5 mg of amitriptyline or placebo twice daily for 14 days. Subsequently in a phase II study 19 adult CF patients were randomly allocated to three treatment groups receiving amitriptyline once daily for 28 days at doses of 25 mg (n=7), 50 mg (n=8), or 75 mg (n=8) or placebo (n=13). The primary outcome was the difference of forced expiratory volume in 1 sec (FEV(1)) at day 14 between amitriptyline and placebo. Primary endpoint measures improved significantly in three of four patients in the pilot study after amitriptyline treatment vs placebo (relative FEV(1): 14.7+/-5%; p = 0.006) and in the 25 mg treatment group of the phase II study (relative FEV(1): 4.0+/-7%; p = 0.048). Amitriptyline was well tolerated in both studies and 96% of the patients completed the studies. Amitriptyline as a novel therapeutic option in patients with CF is safe and seems to be efficacious.
2009 S. Karger AG, Basel.

CONTROLLED TERM: Check Tags: Female; Male
Adult
Amitriptyline: AE, adverse effects
*Amitriptyline: TU, therapeutic use
Anti-Bacterial Agents: AE, adverse effects
*Anti-Bacterial Agents: TU, therapeutic use
*Bacterial Infections: DT, drug therapy
*Cystic Fibrosis: DT, drug therapy
Enzyme Inhibitors: AE, adverse effects
*Enzyme Inhibitors: TU, therapeutic use
Forced Expiratory Volume
Humans
Pseudomonas Infections: DT, drug therapy
Pseudomonas Infections: ET, etiology
Treatment Outcome

CAS REGISTRY NO.: 50-48-6 (Amitriptyline)

CHEMICAL NAME: 0 (Anti-Bacterial Agents); 0 (Enzyme Inhibitors)

L112 ANSWER 14 OF 18 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 7

ACCESSION NUMBER: 2006286269 EMBASE Full-text

TITLE: [The role of sphingolipids in pulmonary disorders].
Die bedeutung von sphingolipiden fur die pathophysiologie der lunge.

AUTHOR: Uhlig, S., Dr. (correspondence)

CORPORATE SOURCE: Institut fur Pharmakologie und Toxikologie, RWTH Aachen, Wendlingweg 2, 52074 Aachen, Germany. stuhlig@ukaachen.de

AUTHOR: Reppien, E.

CORPORATE SOURCE: Forschungszentrum Borstel, Leibniz-Zentrum fur Medizin und Biowissenschaften, Parkallee 22, 23845 Borstel, Germany.

SOURCE: Intensivmedizin und Notfallmedizin, (May 2006) Vol. 43, No. 4, pp. 247-251.
Refs: 38
ISSN: 0175-3851 CODEN: INNOEK

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
005 General Pathology and Pathological Anatomy

LANGUAGE: German

SUMMARY LANGUAGE: English; German

ENTRY DATE: Entered STN: 4 Jul 2006
Last Updated on STN: 4 Jul 2006

ABSTRACT: Sphingolipids such as sphingosine-1-phosphate, ceramide and sphingomyelin are pivotal for the organization of cells and the regulation of many pathophysiological cell responses. Ceramide and sphingomyelin are particularly important for the formation of membrane microdomains. A key step is the conversion of sphingomyelin into ceramide by the sphingomyelinase enzymes. Increased serum concentrations of acid sphingomyelinase are present in a variety of disorders and, for example, correlate with mortality in septic patients. In experimental models inhibition of this enzyme reduces the mortality of sepsis and the extent of pulmonary edema in acute lung injury. The sphingomyelinase/ ceramide pathway is also critical for the elimination of Pseudomonas aeruginosa in the airway tract and for the development of pulmonary emphysema. Thus, the sphingolipid metabolism suggests novel therapeutic targets for the treatment of emphysema, pulmonary infections, sepsis and acute lung injury.

CONTROLLED TERM: Medical Descriptors:
acute lung injury
cell membrane
concentration (parameters)
correlation analysis
enzyme inhibition
human
lipid metabolism
*lung disease
lung edema
lung emphysema
lung infection
mortality
pathophysiology
Pseudomonas aeruginosa
respiratory system
review
sepsis

CONTROLLED TERM: Drug Descriptors:
ceramide
*sphingolipid
sphingomyelin
sphingomyelin phosphodiesterase
sphingosine 1 phosphate

CAS REGISTRY NO.: (sphingomyelin phosphodiesterase) 9031-54-3; (sphingomyelin) 85187-10-6; (sphingosine 1 phosphate) 26993-30-6

L112 ANSWER 15 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:651897 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600653155
TITLE: Ceramide-enriched membrane domains in infectious biology.
AUTHOR(S): Gulbins, E. [Reprint Author]; Grassme, H.
CORPORATE SOURCE: Univ Essen Gesamthsch, Dept Mol Biol, Essen, Germany
SOURCE: Chemistry and Physics of Lipids, (SEP 2006) Vol. 143, No. 1-2, pp. 53.
Meeting Info.: 47th International Conference on Bioscience of Lipids. Pecs, HUNGARY. September 05 -10, 2006. Hungarian Biochem Soc; Hungarian Acad Sci, Biol Res Ctr; Straub Heritage Fdn; European Lipidom Initiat; Int Lecithin & Phospholipid Soc.
CODEN: CPLIA4. ISSN: 0009-3084.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Nov 2006
Last Updated on STN: 29 Nov 2006
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biochemistry studies - Sterols and steroids 10067
Biophysics - Membrane phenomena 10508
Enzymes - General and comparative studies: coenzymes 10802
Morphology and cytology of bacteria 30500
Physiology and biochemistry of bacteria 31000
Virology - General and methods 33502
Medical and clinical microbiology - Virology 36006
INDEX TERMS: Major Concepts
Infection; Enzymology (Biochemistry and Molecular Biophysics); Membranes (Cell Biology)
INDEX TERMS: Parts, Structures, & Systems of Organisms
plasma membrane
INDEX TERMS: Chemicals & Biochemicals
cholesterol; CD40; CD95; ceramide; acid sphingomyelinase [EC 3.1.4.12]; sphingolipid
ORGANISM: Classifier
Picornaviridae 03603
Super Taxa
Positive Sense ssRNA Viruses; Viruses; Microorganisms
Organism Name
Rhinovirus (genus): pathogen
Taxa Notes
Microorganisms, Positive Sense Single-Stranded RNA Viruses, Viruses
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
REGISTRY NUMBER: 57-88-5 (cholesterol)
81271-93-4 (CD95)
104404-17-3 (ceramide)
9031-54-3 (acid sphingomyelinase)
9031-54-3 (EC 3.1.4.12)

L112 ANSWER 16 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:111812 BIOSIS Full-text
DOCUMENT NUMBER: PREV200400114499
TITLE: Role and biophysics of ceramide in bacterial and viral infections.
AUTHOR(S): Gulbins, Erich [Reprint Author]
CORPORATE SOURCE: Dept. of Molecular Biology, University of Duisburg-Essen, Essen, Germany
SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp.

194a. print.
Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004. Biophysical Society.
ISSN: 0006-3495 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Feb 2004
Last Updated on STN: 25 Feb 2004

ABSTRACT:We have recently shown that infection of mammalian lung epithelial cells with P. aeruginosa results in an activation of the acid sphingomyelinase (ASM) and a translocation of the enzyme onto the extracellular leaflet of the cell membrane. The activity of the ASM triggers the release of ceramide that reorganizes small membrane rafts to larger platforms. Ceramide enriched membrane platforms serve to cluster receptor molecules, e.g. CFTR and CD95, that mediate infection with P. aeruginosa. Here, we show that a very similar concept applies to infection of epithelial cells with human rhinovirus and Salmonella typhimurium. Rhinovirus induces an activation of the ASM and the formation of very large ceramide-enriched membrane platforms that co-localize with colera-toxin suggesting that they are formed by the fusion of small membrane rafts. These ceramide-enriched membrane platforms are required for the infection with rhinovirus since destruction of membrane rafts or inhibition of the ASM prevents viral uptake and, thus, infection. Likewise, S. typhimurium is internalized via ceramide-enriched membrane platforms that are formed by activation of the ASM. In addition, the fusion of the intracellular phagosome containing S. typhimurium with phagosomes to form a phagolysosome also requires activity of the acid sphingomyelinase and release of ceramide in the vesicle membrane. Similar data were obtained with BCG mycobacteria. The fusion of intracellular phagosomes that contain the bacteria with lysosomes requires ASM activity and formation of ceramide, while the uptake of BCG seems to be independent of ASM. Thus, ceramide-enriched membrane domains serve as "entrance gates" for several pathogens and, in addition, are critically involved in the fusion of phagosomes with lysosomes.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - General 02502
Biochemistry studies - General 10060
Biochemistry studies - Lipids 10066
Enzymes - General and comparative studies: coenzymes 10802
Morphology and cytology of bacteria 30500
Physiology and biochemistry of bacteria 31000
Virology - General and methods 33502
Medical and clinical microbiology - Virology 36006
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Infection
INDEX TERMS: Parts, Structures, & Systems of Organisms
intracellular phagosomes, fusion; lysosomes; phagosome
INDEX TERMS: Diseases
bacterial infection: bacterial disease
Bacterial Infections (MeSH)
INDEX TERMS: Diseases
viral infection: viral disease
Virus Diseases (MeSH)
INDEX TERMS: Chemicals & Biochemicals
acid sphingomyelinase [EC 3.1.4.12]: activation; ceramide: formation
ORGANISM: Classifier

Enterobacteriaceae 06702
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Salmonella typhimurium (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGANISM: Classifier
Picornaviridae 03603
Super Taxa
Positive Sense ssRNA Viruses; Viruses; Microorganisms
Organism Name
Rhinovirus (genus): pathogen
Taxa Notes
Microorganisms, Positive Sense Single-Stranded RNA Viruses, Viruses
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
REGISTRY NUMBER: 9031-54-3 (acid sphingomyelinase)
9031-54-3 (EC 3.1.4.12)
104404-17-3 (ceramide)

L112 ANSWER 17 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:549686 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300538164
TITLE: Raft ceramide in molecular medicine.
AUTHOR(S): Gulbins, Erich [Reprint Author]; Kolesnick, Richard
CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Hufelandstrasse 55, Essen, 45122, Germany
erich.gulbins@uni-essen.de
SOURCE: Oncogene, (13 October 2003) Vol. 22, No. 45, pp. 7070-7077. print.
ISSN: 0950-9232 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Nov 2003
Last Updated on STN: 19 Nov 2003
ABSTRACT:Ceramide, generated by the action of acid sphingomyelinase (ASM), has emerged as a biochemical mediator of stimuli as diverse as ionizing radiation, chemotherapy, UVA light, heat, CD95, reperfusion injury, as well as infection with some pathogenic bacteria and viruses. ASM activity is also crucial for developmental programmed cell death of oocytes by apoptosis. Recently, we proposed a comprehensive model that might explain these diverse functions of ceramide: Upon contacting the relevant stimuli, ASM translocates into and generates ceramide within distinct plasma membrane sphingolipid-enriched microdomains termed rafts. Ceramide, which manifests a unique biophysical property, the capability to self-associate through hydrogen bonding, provides the driving force that results in the coalescence of microscopic rafts into large-membrane macrodomains. These structures serve as platforms for protein concentration and oligomerization, transmitting signals

across the plasma membrane. Preliminary data suggest that manipulation of ceramide metabolism and/or the function of ceramide-enriched membrane platforms may present novel therapeutic opportunities for the treatment of cancer, degenerative disorders, pathogenic infections or cardiovascular diseases.

CONCEPT CODE: Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biophysics - Membrane phenomena 10508
Enzymes - General and comparative studies: coenzymes 10802
Physiology - General 12002
Pathology - General 12502
Cardiovascular system - Heart pathology 14506
Cardiovascular system - Blood vessel pathology 14508
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Morphology and cytology of bacteria 30500
Physiology and biochemistry of bacteria 31000
Virology - General and methods 33502
Immunology - Immunopathology, tissue immunology 34508
Medical and clinical microbiology - Bacteriology 36002
Medical and clinical microbiology - Virology 36006
Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Membranes (Cell Biology); Pathology; Physiology

INDEX TERMS: Parts, Structures, & Systems of Organisms
plasma membrane

INDEX TERMS: Diseases
autoimmune syndromes: immune system disease

INDEX TERMS: Diseases
bacterial infection: bacterial disease
Bacterial Infections (MeSH)

INDEX TERMS: Diseases
cancer: neoplastic disease
Neoplasms (MeSH)

INDEX TERMS: Diseases
cardiovascular disease: heart disease, vascular disease
Cardiovascular Diseases (MeSH)

INDEX TERMS: Diseases
degenerative disorders: disease-miscellaneous

INDEX TERMS: Diseases
viral infection: viral disease
Virus Diseases (MeSH)

INDEX TERMS: Chemicals & Biochemicals
CD95; acid sphingomyelinase [EC 3.1.4.12]: activity; ceramide: functions, generation, hydrogen bonding, self-association; lipid rafts: coalescence, sphingolipid-enriched microdomains

INDEX TERMS: Methods & Equipment
chemotherapy: clinical techniques, therapeutic and prophylactic techniques; molecular model: mathematical and computer techniques

INDEX TERMS: Miscellaneous Descriptors
UVA light; death receptor-mediated apoptosis; heart; ionizing radiation; molecular medicine; oligomerization;

physiological cell turnover; protein concentration; reperfusion injury; signal transmission

ORGANISM: Classifier
Bacteria 05000
Super Taxa
Microorganisms
Organism Name
bacteria (common): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common): animal model
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGANISM: Classifier
Neisseriaceae 06507
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Neisseria gonorrhoeae (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium falciparum (species): parasite
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans

ORGANISM: Classifier
Viruses 03000
Super Taxa
Microorganisms
Organism Name
Virus (common): pathogen

Taxa Notes
Microorganisms, Viruses
REGISTRY NUMBER: 81271-93-4 (CD95)
9031-54-3 (acid sphingomyelinase)
9031-54-3 (EC 3.1.4.12)
104404-17-3 (ceramide)

L112 ANSWER 18 OF 18 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:596410 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200596410
TITLE: Molecular mechanisms of pulmonary P. aeruginosa infections.
AUTHOR(S): Gulbins, E. [Reprint author]; Grassme, H. [Reprint author]
CORPORATE SOURCE: Dept. of Molecular Biology, University of Essen, Hufelandstrasse 55, 45122, Essen, Germany
SOURCE: International Journal of Molecular Medicine, (2002) Vol. 10, No. Supplement 1, pp. S95. print.
Meeting Info.: 7th World Congress on Advances in Oncology and the 5th International Symposium on Molecular Medicine. Hersonissos, Crete, Greece. October 10-12, 2002.
ISSN: 1107-3756.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Nov 2002
Last Updated on STN: 20 Nov 2002
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Cytology - Human 02508
Genetics - Human 03508
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Enzymes - General and comparative studies: coenzymes 10802
Metabolism - Metabolic disorders 13020
Digestive system - Pathology 14006
Respiratory system - Physiology and biochemistry 16004
Respiratory system - Pathology 16006
Physiology and biochemistry of bacteria 31000
Medical and clinical microbiology - Bacteriology 36002
INDEX TERMS: Major Concepts
Infection; Respiratory System (Respiration)
INDEX TERMS: Parts, Structures, & Systems of Organisms
lung epithelial cells: respiratory system, apoptosis
INDEX TERMS: Diseases
cystic fibrosis: digestive system disease, genetic disease, metabolic disease, respiratory system disease
Cystic Fibrosis (MeSH)
INDEX TERMS: Diseases
pulmonary Pseudomonas aeruginosa infection: bacterial disease, respiratory system disease, etiology
Pseudomonas Infections (MeSH)
INDEX TERMS: Chemicals & Biochemicals
CD95; CD95 ligand; acid sphingomyelinase; ceramide
INDEX TERMS: Miscellaneous Descriptors
molecular mechanisms; Meeting Abstract
ORGANISM: Classifier

Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM:
Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
P. aeruginosa [Pseudomonas aeruginosa]: pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER:
81271-93-4 (CD95)
9031-54-3 (acid sphingomyelinase)
104404-17-3 (ceramide)

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L93        42657 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  PSEUDOMONAS AERUGINOSA
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L97         3038 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  ?SPHINGOMYELINAS?/BI
L98           30 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L93 AND L97
L103           1 SEA FILE=REGISTRY SPE=ON  ABB=ON  PLU=ON  ACID SPHINGOMYELINASE
                 /CN
L108          24 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L103 AND L93
L109          30 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  L98 OR L108


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L113        19 L109 NOT L106

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L97         3038 SEA FILE=ZCAPLUS SPE=ON  ABB=ON  PLU=ON  ?SPHINGOMYELINAS?/BI
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L99           64 SEA L98


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L114        34 L99 NOT L111

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PROCESSING COMPLETED FOR L114
L115         27 DUP REM L113 L114 (26 DUPLICATES REMOVED)
                ANSWERS '1-19' FROM FILE ZCAPLUS
                ANSWER '20' FROM FILE MEDLINE
                ANSWER '21' FROM FILE EMBASE
                ANSWERS '22-27' FROM FILE BIOSIS

=> d iall hitstr L115 1-19; d iall L115 20-27

L115 ANSWER 1 OF 27  ZCAPLUS  COPYRIGHT 2009 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2009:598926  ZCAPLUS  Full-text
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DOCUMENT NUMBER: 151:53416
ENTRY DATE: Entered STN: 19 May 2009
TITLE: A complex extracellular sphingomyelinase of Pseudomonas aeruginosa inhibits angiogenesis by selective cytotoxicity to endothelial cells
AUTHOR(S): Vasil, Michael L.; Stonehouse, Martin J.; Vasil, Adriana I.; Wadsworth, Sandra J.; Goldfine, Howard; Bolcome, Robert E., III; Chan, Joanne
CORPORATE SOURCE: Department of Microbiology, Anschutz Medical Center, University of Colorado Denver, Aurora, CO, USA
SOURCE: PLoS Pathogens (2009), 5(5), No pp. given
CODEN: PPLACN; ISSN: 1553-7374
URL: http://www.plospathogens.org/article/fetchObjectAttachment.action?uri=info%3Adoi%2F10.1371%2Fjournal.ppat.1000420&representation=PDF
PUBLISHER: Public Library of Science
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
CLASSIFICATION: 14-3 (Mammalian Pathological Biochemistry)
ABSTRACT:
The hemolytic phospholipase C (PlcHR) expressed by P. aeruginosa is the original member of a phosphoesterase superfamily, which includes phosphorylcholine-specific phospholipases C (PC-PLC) produced by frank and opportunistic pathogens. PlcHR, but not all its family members, is also a potent sphingomyelinase (SMase). Data presented herein indicate that picomolar (pM) concns. of PlcHR are selectively lethal to endothelial cells (EC). An RGD motif of PlcHR contributes to this selectivity. Peptides containing an RGD motif (i.e., GRGDS), but not control peptides (i.e., GDGRS), block the effects of PlcHR on calcium signaling and cytotoxicity to EC. Moreover, RGD variants of PlcHR (e.g., RGE, KGD) are reduced in their binding and toxicity, but retain the enzymic activity of the wild type PlcHR. PlcHR also inhibits several EC-dependent in vitro assays (i.e., EC migration, EC invasion, and EC tubule formation), which represent key processes involved in angiogenesis (i.e., formation of new blood vessels from existing vasculature). Finally, the impact of PlcHR in an in vivo model of angiogenesis in transgenic zebrafish, and ones treated with an antisense morpholino to knock down a key blood cell regulator, were evaluated because in vitro assays cannot fully represent the complex processes of angiogenesis. As little as 2 ng/embryo of PlcHR was lethal to .apprx.50% of EGFP-labeled EC at 6 h after injection of embryos at 48 hpf (hours post-fertilization). An active site mutant of PlcHR (Thr178Ala) exhibited 120-fold reduced inhibitory activity in the EC invasion assay, and 20 ng/embryo elicited no detectable inhibitory activity in the zebrafish model. Taken together, these observations are pertinent to the distinctive vasculitis and poor wound healing associated with P. aeruginosa sepsis and suggest that the potent antiangiogenic properties of PlcHR are worthy of further investigation for the treatment of diseases where angiogenesis contributes pathol. conditions (e.g., vascularization of tumors, diabetic retinopathy).

SUPPL. TERM: extracellular sphingomyelinase Pseudomonas angiogenesis inhibition endothelium cytotoxicity
INDEX TERM: Protein motifs
(RGD; extracellular sphingomyelinase (hemolytic phospholipase C, PlcHR) of Pseudomonas aeruginosa inhibits angiogenesis by selective cytotoxicity to vascular endothelium)
INDEX TERM: Angiogenesis
Cytotoxicity
Pseudomonas aeruginosa
Sepsis
Signal transduction

Vascular endothelium
Vasculitis
Wound healing
(extracellular sphingomyelinase (hemolytic phospholipase C, PlcHR) of Pseudomonas aeruginosa inhibits angiogenesis by selective cytotoxicity to vascular endothelium)

INDEX TERM: 7440-70-2, Calcium, biological studies 9031-54-3, Sphingomyelinase 102784-33-8, Phosphatidylcholine-hydrolyzing phospholipase C
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(extracellular sphingomyelinase (hemolytic phospholipase C, PlcHR) of Pseudomonas aeruginosa inhibits angiogenesis by selective cytotoxicity to vascular endothelium)

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IT 9031-54-3, Sphingomyelinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(extracellular sphingomyelinase (hemolytic phospholipase C, PlcHR) of Pseudomonas aeruginosa inhibits angiogenesis by selective cytotoxicity to vascular endothelium)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 2 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2008:1183621 ZCAPLUS Full-text
DOCUMENT NUMBER: 149:396432
ENTRY DATE: Entered STN: 02 Oct 2008
TITLE: Ceramide-Enriched Membrane Domains in Red Blood Cells and the Mechanism of Sphingomyelinase-Induced Hot-Cold Hemolysis
AUTHOR(S): Montes, L.-Ruth; Lopez, David J.; Sot, Jesus; Bagatolli, Luis A.; Stonehouse, Martin J.; Vasil, Michael L.; Wu, Bill X.; Hannun, Yusuf A.; Goni, Felix M.; Alonso, Alicia
CORPORATE SOURCE: Unidad de Biofisica (Centro Mixto CSIC-UPV/EHU), Departamento de Bioquimica, Universidad del Pais

Vasco, Bilbao, 48080, Spain
SOURCE: Biochemistry (2008), 47(43), 11222-11230
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 6-6 (General Biochemistry)
Section cross-reference(s): 13

ABSTRACT:
Hot-cold hemolysis is the phenomenon whereby red blood cells, preincubated at 37° in the presence of certain agents, undergo rapid hemolysis when transferred to 4°. The mechanism of this phenomenon is not understood. PlcHR2, a phospholipase C/sphingomyelinase from Pseudomonas aeruginosa, that is the prototype of a new phosphatase superfamily, induces hot-cold hemolysis. We found that the sphingomyelinase, but not the phospholipase C activity, is essential for hot-cold hemolysis because the phenomenon occurs not only in human erythrocytes that contain both phosphatidylcholine (PC) and sphingomyelin (SM) but also in goat erythrocytes, which lack PC. However, in horse erythrocytes, with a large proportion of PC and almost no SM, hot-cold hemolysis induced by PlcHR2 is not observed Fluorescence microscopy observations confirm the formation of ceramide-enriched domains as a result of PlcHR2 activity. After cooling down to 4°, the erythrocyte ghost membranes arising from hemolysis contain large, ceramide-rich domains. We suggest that formation of these rigid domains in the originally flexible cell makes it fragile, thus highly susceptible to hemolysis. We also interpret the slow hemolysis observed at 37° as a phenomenon of gradual release of aqueous contents, induced by the sphingomyelinase activity, as described by Ruiz-Arguello before. These hypotheses are supported by the fact that ceramidase, which is known to facilitate slow hemolysis at 37°, actually hinders hot-cold hemolysis. Differential scanning calorimetry of erytrocyte membranes treated with PlcHR2 demonstrates the presence of ceramide-rich domains that are rigid at 4° but fluid at 37°. Ceramidase treatment causes the disapperance of the calorimetric signal assigned to ceramide-rich domains. Finally, in liposomes composed of SM, PC, and cholesterol, which exhibit slow release of aqueous contents at 37°, addition of 10 mol % ceramide and transfer to 4° cause a large increase in the rate of solute efflux.

SUPPL. TERM: ceramide membrane erythrocyte sphingomyelinase hemolysis human goat horse
INDEX TERM: Erythrocyte
(cell membrane; ceramide-enriched membrane domains in red blood cells and the mechanism of sphingomyelinase -induced hot-cold hemolysis)
INDEX TERM: Capra hircus
Equus caballus
Erythrocyte
Goat
Hemolysis
Horse
Human
(ceramide-enriched membrane domains in red blood cells and the mechanism of sphingomyelinase-induced hot-cold hemolysis)
INDEX TERM: Ceramides
Phosphatidylcholines, biological studies
Sphingomyelins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(ceramide-enriched membrane domains in red blood cells and the mechanism of sphingomyelinase-induced hot-cold hemolysis)

INDEX TERM: Cell membrane
(erythrocyte; ceramide-enriched membrane domains in red blood cells and the mechanism of sphingomyelinase -induced hot-cold hemolysis)

INDEX TERM: 57-88-5, Cholesterol, biological studies 9031-54-3, Sphingomyelinase 56467-83-5, Ceramidase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide-enriched membrane domains in red blood cells and the mechanism of sphingomyelinase-induced hot-cold hemolysis)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

DATE LAST CITED: Date last citing reference entered STN: 26 May 2009

OS.CITING.REFS: CAPLUS 2009:598926; 2009:44158

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IT 9031-54-3, Sphingomyelinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide-enriched membrane domains in red blood cells and the mechanism of sphingomyelinase-induced hot-cold hemolysis)

RN 9031-54-3 ZCAPLUS

CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 3 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2007:204082 ZCAPLUS Full-text
DOCUMENT NUMBER: 146:375696
ENTRY DATE: Entered STN: 23 Feb 2007
TITLE: Ceramidase Enhances Phospholipase C-induced Hemolysis by Pseudomonas aeruginosa
AUTHOR(S): Okino, Nozomu; Ito, Makoto
CORPORATE SOURCE: Department of Bioscience and Biotechnology, Graduate School of Bioresource and Bioenvironmental Sciences, Kyushu University, 6-10-1, Hakozaki, Higashi-ku, Fukuoka, 812-8581, Japan
SOURCE: Journal of Biological Chemistry (2007), 282(9), 6021-6030
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 10-6 (Microbial, Algal, and Fungal Biochemistry)
ABSTRACT:
We previously reported the purification, mol. cloning, and characterization of a neutral ceramidase from Pseudomonas aeruginosa strain AN17 (Okino, N., Tani, M., Imayama, S., and Ito, M. (1998) J. Biol. Chemical 273, 14368-14373; Okino, N., Ichinose, S., Omori, A., Imayama, S., Nakamura, T., and Ito, M. (1999) J. Biol. Chemical 274, 36616-36622). Interestingly, the gene encoding the enzyme is adjacent to that encoding hemolytic phospholipase C (plcH) in the genome of Pseudomonas aeruginosa, which is a well known pathogen for opportunistic infections. We report here that simultaneous production of PlcH and ceramidase was induced by several lipids and PlcH-induced hemolysis was significantly enhanced by the action of the ceramidase. When the strain was cultured with sphingomyelin or phosphatidylcholine, production of both enzymes drastically increased, causing the increase of hemolytic activity in the cell-free culture supernatant. Ceramide and sphingosine were also effective in promoting the production of ceramidase but not that of PlcH. Furthermore, we found that the hemolytic activity of a Bacillus cereus sphingomyelinase was significantly enhanced by addition of a recombinant Pseudomonas ceramidase. TLC anal. of the erythrocytes showed that ceramide produced from sphingomyelin by the sphingomyelinase was partly converted to sphingosine by the ceramidase. A ceramidase-null mutant strain caused much less hemolysis of sheep erythrocytes than did the wild-type strain. Sphingosine was detected in the erythrocytes co-cultured with the wild-type strain but not the mutant strain. Finally, we found that the enhancement of PlcH-induced hemolysis by the ceramidase occurred in not only sheep but also human erythrocytes. These results may indicate that the ceramidase enhances the PlcH-induced cytotoxicity and provide new insights into the role of sphingolipid-degrading enzymes in the pathogenicity of P. aeruginosa.

SUPPL. TERM: ceramidase phospholipase C erythrocyte hemolysis Pseudomonas virulence; sphingomyelin phosphatidylcholine ceramide sphingosine erythrocyte membrane Pseudomonas hemolysis
INDEX TERM: Erythrocyte
(cell membrane; ceramidase induced by several lipids enhances phospholipase C-induced hemolysis in sheep and human erythrocytes by Pseudomonas aeruginosa)
INDEX TERM: Hemolysis
Human

Pseudomonas aeruginosa
Virulence (microbial)
(ceramidase induced by several lipids enhances phospholipase C-induced hemolysis in sheep and human erythrocytes by Pseudomonas aeruginosa
)
INDEX TERM: Ceramides
Phosphatidylcholines, biological studies
Phospholipids, biological studies
Sphingolipids
Sphingomyelins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramidase induced by several lipids enhances phospholipase C-induced hemolysis in sheep and human erythrocytes by Pseudomonas aeruginosa
)
INDEX TERM: Cell membrane
(erythrocyte; ceramidase induced by several lipids enhances phospholipase C-induced hemolysis in sheep and human erythrocytes by Pseudomonas aeruginosa)
INDEX TERM: Bacillus cereus
(sphingomyelinase; ceramidase induced by several lipids enhances phospholipase C-induced hemolysis in sheep and human erythrocytes by Pseudomonas aeruginosa)
INDEX TERM: 123-78-4, Sphingosine 3102-57-6, C2-Ceramide 9001-86-9, Phospholipase C 9031-54-3, Sphingomyelinase 37289-06-8, Neutral ceramidase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramidase induced by several lipids enhances phospholipase C-induced hemolysis in sheep and human erythrocytes by Pseudomonas aeruginosa
)
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 08 Oct 2009
OS.CITING.REFS: CAPLUS 2009:1026936; 2009:368541; 2008:1183621; 2008:1064754; 2007:1230744
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD.
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IT 9031-54-3, Sphingomyelinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramidase induced by several lipids enhances phospholipase C-induced hemolysis in sheep and human erythrocytes by Pseudomonas aeruginosa)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 4 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2007:1158027 ZCAPLUS Full-text
DOCUMENT NUMBER: 148:26365
ENTRY DATE: Entered STN: 15 Oct 2007
TITLE: Leakage-free membrane fusion induced by the hydrolytic activity of PlcHR2, a novel phospholipase C/sphingomyelinase from Pseudomonas aeruginosa
AUTHOR(S): Montes, L.-Ruth; Ibarguren, Maitane; Goni, Felix M.; Stonehouse, Martin; Vasil, Michael L.; Alonso, Alicia
CORPORATE SOURCE: Unidad de Biofisica (Centro Mixto CSIC-UPV/EHU), and Departamento de Bioquimica, Universidad del Pais Vasco, Bilbao, 48080, Spain
SOURCE: Biochimica et Biophysica Acta, Biomembranes (2007), 1768(10), 2365-2372

CODEN: BBBMBS; ISSN: 0005-2736
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 7-8 (Enzymes)

ABSTRACT:
PlcHR2 is the paradigm member of a novel phospholipase C/phosphatase superfamily, with members in a variety of bacterial species. This paper describes the phospholipase C and sphingomyelinase activities of PlcHR2 when the substrate is in the form of large unilamellar vesicles, and the subsequent effects of lipid hydrolysis on vesicle and bilayer stability, including vesicle fusion. PlcHR2 cleaves phosphatidylcholine and sphingomyelin at equal rates, but is inactive on phospholipids that lack choline head groups. Calcium in the millimolar range does not modify in any significant way the hydrolytic activity of PlcHR2 on choline-containing phospholipids. The catalytic activity of the enzyme induces vesicle fusion, as demonstrated by the concomitant observation of intervesicular total lipid mixing, inner monolayer-lipid mixing, and aqueous contents mixing. No release of vesicular contents is detected under these conditions. The presence of phosphatidylserine in the vesicle composition does not significantly modify PlcHR2-induced liposome aggregation, as long as Ca2+ is present, but completely abolishes fusion, even in the presence of the cation. Each of the various enzyme-induced phenomena have their characteristic latency periods, that increase in the following order: lipid hydrolysis < vesicle aggregation < total lipid mixing < inner lipid mixing < contents mixing. Concomitant measurements of the threshold diacylglyceride + ceramide concns. in the bilayer show that late events such as lipid mixing require a higher concentration
of PlcHR2 products than early events such as aggregation. When the above results are examined in the context of the membrane effects of other phospholipid phosphocholine hydrolases it can be concluded that aggregation is necessary, but not sufficient for membrane fusion to occur, that diacylglycerol is far more fusogenic than ceramide, and that vesicle membrane permeabilization occurs independently from vesicle fusion.

SUPPL. TERM: PlcHR2 Pseudomonas phospholipase PLC sphingomyelinase membrane fusion
INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(PlcHR2; hydrolytic activity of phospholipase C/ sphingomyelinase PlcHR2 from P. aeruginosa induces leakage-free membrane fusion)
INDEX TERM: Membrane, biological
(bilayer, fusion; hydrolytic activity of phospholipase C/ sphingomyelinase PlcHR2 from P. aeruginosa induces leakage-free membrane fusion)
INDEX TERM: Pseudomonas aeruginosa
(hydrolytic activity of phospholipase C/ sphingomyelinase PlcHR2 from P. aeruginosa induces leakage-free membrane fusion)
INDEX TERM: Fusion, biological
(membrane; hydrolytic activity of phospholipase C/ sphingomyelinase PlcHR2 from P. aeruginosa induces leakage-free membrane fusion)
INDEX TERM: Phosphatidylserines
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(neg. effect on fusion; hydrolytic activity of phospholipase C/sphingomyelinase PlcHR2 from P. aeruginosa induces leakage-free

membrane fusion)
INDEX TERM: 9031-54-3, Sphingomyelinase
102784-33-8, Phospholipase C
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(hydrolytic activity of phospholipase C/ sphingomyelinase PlcHR2 from P. aeruginosa induces leakage-free membrane fusion)
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 10 Jul 2009
OS.CITING.REFS: CAPLUS 2009:515485; 2009:598926; 2008:1183621; 2008:1128577
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD.
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IT 9031-54-3, Sphingomyelinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydrolytic activity of phospholipase C/sphingomyelinase PlcHR2 from P. aeruginosa induces leakage-free membrane fusion)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 5 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2006:441041 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:22455
ENTRY DATE: Entered STN: 11 May 2006
TITLE: Acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors
AUTHOR(S): Popova, Taissia G.; Millis, Bryan; Bradburne, Chris; Nazarenko, Svetlana; Bailey, Charles; Chandhoke, Vikas; Popov, Serguei G.
CORPORATE SOURCE: National Center for Biodefense and Infectious Diseases, George Mason University, Manassas, VA, 20110, USA
SOURCE: BMC Microbiology (2006), 6, No pp. given
CODEN: BMMIBC; ISSN: 1471-2180
URL: http://www.biomedcentral.com/content/pdf/1471-2180-6-8.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
CLASSIFICATION: 4-5 (Toxicology)
ABSTRACT:
Background: It has been recently reported that major pathogens Staphylococcus aureus and Pseudomonas aeruginosa accelerate a normal process of cell surface syndecan-1 (Syndl) ectodomain shedding as a mechanism of host damage due to the production of shedding-inducing virulence factors. We tested if acceleration of Syndl shedding takes place in vitro upon treatment of epithelial cells with B. anthracis hemolysins, as well as in vivo during anthrax infection in mice. Results: The isolated anthrax hemolytic proteins AnlB (sphingomyelinase) and AnlO (cholesterol-binding pore-forming factor), as well as ClnA (B. cereus homolog of B. anthracis phosphatidyl choline-preferring phospholipase C) cause accelerated shedding of Syndl and E-cadherin from epithelial cells and compromise epithelial barrier integrity within a few hours. In comparison with hemolysins in a similar range of concns., anthrax lethal toxin (LT) also accelerates shedding albeit at slower rate. Individual components of LT, lethal factor and protective antigen are inactive with regard to shedding. Inhibition expts. favor a hypothesis that activities of tested bacterial shedding inducers converge on the stimulation of cytoplasmic tyrosine kinases of the Syk family, ultimately leading to activation of cellular sheddase. Both LT and AnlO modulate ERK1/2 and p38 MAPK signaling pathways, while JNK pathway seems to be irrelevant to accelerated shedding. Accelerated shedding of Syndl also takes place in DBA/2 mice challenged with Bacillus anthracis (Sterne) spores. Elevated levels of shed ectodomain are readily detectable in circulation after 24 h. Conclusion: The

concerted acceleration of shedding by several virulence factors could represent a new pathogenic mechanism contributing to disruption of epithelial or endothelial integrity, hemorrhage, edema and abnormal cell signaling during anthrax infection.

SUPPL. TERM: anthrax hemolytic protein Bacillus syndecan mammary epithelium virulence

INDEX TERM: Cadherins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(1; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors)

INDEX TERM: Syndecans
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(1; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors and Bacillus anthracis hemolysins)

INDEX TERM: Hemolysins
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(An10; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic proteins)

INDEX TERM: Hemolysins
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(ClnA; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic proteins)

INDEX TERM: Cell death
Phosphorylation, biological
(acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors)

INDEX TERM: Bacillus anthracis
Signal transduction, biological
Virulence (microbial)
(acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors and Bacillus anthracis hemolysins)

INDEX TERM: Toxins
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(anthrax lethal factor; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors)

INDEX TERM: Toxins
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(anthrax protective antigen; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors)

INDEX TERM: Toxins
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(anthrax; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors)

INDEX TERM: Infection
(anthrax; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors and Bacillus anthracis hemolysins)

INDEX TERM: Mammary gland

(epithelium; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors)

INDEX TERM: Epithelium
(mammary; acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors)

INDEX TERM: 9031-54-3, Sphingomyelinase
ROLE: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic proteins)

INDEX TERM: 9001-60-9, Lactate dehydrogenase 137632-08-7, ERK2 kinase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors)

INDEX TERM: 137632-07-6, ERK1 kinase 165245-96-5, p38 MAPK
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors and Bacillus anthracis hemolysins)

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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IT 9031-54-3, Sphingomyelinase
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic proteins)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 6 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2003:662571 ZCAPLUS Full-text
DOCUMENT NUMBER: 139:288024
ENTRY DATE: Entered STN: 25 Aug 2003
TITLE: Purification, Characterization, and Identification of a Sphingomyelin Synthase from Pseudomonas aeruginosa: PlcH is a Multifunctional Enzyme
AUTHOR(S): Luberto, Chiara; Stonehouse, Martin J.; Collins, Elizabeth A.; Marchesini, Norma; El-Bawab, Samer; Vasil, Adriana I.; Vasil, Michael L.; Hannun, Yusuf A.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, SC, 29425, USA
SOURCE: Journal of Biological Chemistry (2003), 278(35), 32733-32743
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 7-2 (Enzymes)
Section cross-reference(s): 10

ABSTRACT:
Sphingomyelin synthase is the enzyme that synthesizes sphingomyelin (SM) in mammalian cells by transferring a phosphorylcholine moiety from phosphatidylcholine to ceramide. Despite its importance, the gene and/or the protein responsible for this activity has not yet been identified. Here we report the purification, identification, and biochem. characterization of an

enzymic
activity that synthesizes SM in Pseudomonas aeruginosa. SM synthase-like activity was found secreted in the culture medium of P. aeruginosa, strains PA01 and PAK, whereas it could not be detected in cultures of Escherichia coli. From the medium of PAK cultures, SM synthase was purified through sequential chromatog. columns. After separation on polyacrylamide-SDS gels and visualization by silver staining, the purified enzyme showed two bands, one of .apprx.75 kDa and one of 30-35 kDa. Interestingly, the highly purified SM synthase preparation also showed neutral sphingomyelinase activity. We therefore investigated whether the protein we purified as SM synthase could actually be the previously identified PlcH, a 78-kDa phospholipase C known to hydrolyze phosphatidylcholine and SM in P. aeruginosa. First, the purified SM synthase preparation contained a 78-kDa protein that reacted with monoclonal antibodies raised against purified PlcH. Second, purified PlcH showed SM synthase activity. Third, using different knockout mutant strains for the PlcH operon, PlcH was found to be necessary for SM synthase activity in P. aeruginosa. Interestingly, SM synthase activity was specific to the Pseudomonas PlcH as other bacterial phospholipases did not display SM synthase activity. Biochem. studies on the Pseudomonas SM synthase confirmed that it is a transferase, similar to the mammalian enzyme, that specifically recognizes the choline head-group and the primary hydroxyl on ceramide. This SM synthase did not have reverse transferase activity. In conclusion, the Pseudomonas PlcH also exerts SM synthase activity; therefore, for the first time, we have identified a structural gene for a SM synthase.

SUPPL. TERM: sphingomyelin synthase Pseudomonas aeruginosa PlcH sphingomyelinase phosphatidylcholine

INDEX TERM: Pseudomonas aeruginosa
(PA01 and PAK; purification, characterization, and identification of a sphingomyelin synthase/sphingomyelinase (PlcH) from Pseudomonas aeruginosa)

INDEX TERM: Operon
(PlcH, knockout of; purification, characterization, and identification of a sphingomyelin synthase/sphingomyelinase (PlcH) from Pseudomonas aeruginosa)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(PlcHR2 (sphingomyelin synthase accessory protein); purification, characterization, and identification of a sphingomyelin synthase/sphingomyelinase (PlcH) from Pseudomonas aeruginosa)

INDEX TERM: Structure-activity relationship
(enzyme substrate; purification, characterization, and identification of a sphingomyelin synthase/sphingomyelinase (PlcH) from Pseudomonas aeruginosa)

INDEX TERM: Michaelis constant
(purification, characterization, and identification of a sphingomyelin synthase/sphingomyelinase (PlcH) from Pseudomonas aeruginosa)

INDEX TERM: Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylinositols
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(purification, characterization, and identification of a sphingomyelin synthase/sphingomyelinase (PlcH) from Pseudomonas aeruginosa)

INDEX TERM: 9031-54-3P, Neutral sphingomyelinase
58703-97-2P, Sphingomyelin synthase
ROLE: BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(PlcH; purification, characterization, and identification of a sphingomyelin synthase/sphingomyelinase (PlcH) from Pseudomonas aeruginosa)

OS.CITING REF COUNT: 17 THERE ARE 17 CAPLUS RECORDS THAT CITE THIS RECORD (17 CITINGS)

DATE LAST CITED: Date last citing reference entered STN: 10 Jul 2009

OS.CITING.REFS: CAPLUS 2009:515485; 2009:130629; 2007:1230744; 2007:1158027; 2007:353824; 2006:1022367; 2006:1022279; 2006:1008155; 2006:957897; 2006:914147; 2006:23623; 2005:690131; 2004:717438; 2004:425134; 2004:346518; 2004:151876; 2004:103980

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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IT 9031-54-3P, Neutral sphingomyelinase
RL: BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(PlcH; purification, characterization, and identification of a sphingomyelin
synthase/sphingomyelinase (PlcH) from Pseudomonas aeruginosa)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 7 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 7

ACCESSION NUMBER:	1996:455186 ZCAPLUS Full-text
DOCUMENT NUMBER:	125:134324
ORIGINAL REFERENCE NO.:	125:24972h,24973a
ENTRY DATE:	Entered STN: 01 Aug 1996
TITLE:	Biochemical and molecular analysis of phospholipase C and phospholipase D activity in mycobacteria
AUTHOR(S):	Johansen, Kristine A.; Gill, Ronald E.; Vasil, Michael L.
CORPORATE SOURCE:	Dep. Microbiol., Univ. Colorado Health Sci. Cent., Denver, CO, 80262, USA
SOURCE:	Infection and Immunity (1996), 64(8), 3259-3266 CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER:	American Society for Microbiology
DOCUMENT TYPE:	Journal
LANGUAGE:	English
CLASSIFICATION:	3-3 (Biochemical Genetics) Section cross-reference(s): 7, 10, 14

ABSTRACT:
Resurgence of mycobacterial infections in the United States has led to an intense effort to identify potential virulence determinants in the genus Mycobacterium, particularly ones that would be associated with the more virulent species (e.g., Mycobacterium tuberculosis). Thin-layer chromatog. (TLC) using radiolabeled phosphatidylcholine and sphingomyelin as substrates indicated that cell exts. of M. tuberculosis contain both phospholipase C (PLC) and phospholipase D (PLD) activities. In contrast, only PLD activity was detected in cell exts. of M. smegmatis. Neither activity was detected in cell-free culture supernatants from these organisms. We and others recently identified two open reading frames in M. tuberculosis with the potential to encode proteins which are highly homologous to the nonhemolytic (PlcN) and hemolytic

(PlcH) phospholipase C enzymes of Pseudomonas aeruginosa. In contrast to the plc genes in P. aeruginosa, which are considerably distal to each other (min 34 and 64 on the chromosome), the mycobacterial genes, designated mpcA and mpcB, are tandemly arranged in the same relative orientation and separated by only 191 bp. Both the mpcA and the mpcB genes were individually cloned in M. smegmatis, and PLC activity was expressed from each gene in this organism. Hybridization expts. using the mpcA and the mpcB genes as probes under conditions of moderate stringency identified sequences homologous to these genes in M. bovis, M. bovis BCG, and M. marinum but not in several other Mycobacterium species, including M. smegmatis, M. avium, and M. intracellulare. TLC anal. using radiolabeled substrates indicated that M. bovis and M. marinum cell exts. contain PLC and PLD activities, but only PLD activity was detected in M. bovis BCG cell exts. Sphingomyelinase activity was also detected in whole-cell exts. of M. tuberculosis, M. marinum, M. bovis, and M. bovis BCG, but this activity was not detected in exts. of M. smegmatis. Sphingomyelinase activity was detected in cell exts. from M. smegmatis harboring either recombinant mpcA or mpcB. These data indicate that PLC and sphingomyelinase activities are associated with the most virulent mycobacterial species, while PLD activity was detected in both virulent and saprophytic strains.

SUPPL. TERM: mycobacterium phospholipase C D virulence; sequence gene mpcA pmcB phospholipase Mycobacterium

INDEX TERM: Mycobacterium
Mycobacterium BCG
Mycobacterium avium
Mycobacterium bovis
Mycobacterium intracellulare
Mycobacterium marinum
Mycobacterium smegmatis
Mycobacterium tuberculosis
(biochem. and mol. anal. of phospholipase C and phospholipase D activity in mycobacteria)

INDEX TERM: Gene, microbial
ROLE: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(mpcA; biochem. and mol. anal. of phospholipase C and phospholipase D activity in mycobacteria)

INDEX TERM: Gene, microbial
ROLE: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(mpcB; biochem. and mol. anal. of phospholipase C and phospholipase D activity in mycobacteria)

INDEX TERM: Deoxyribonucleic acid sequences
(of genes mpcA and mpcB from Mycobacterium tuberculosis)

INDEX TERM: Protein sequences
(of phospholipase C isoenzymes from Mycobacterium tuberculosis)

INDEX TERM: Microbial virulence
(phospholipases C and D and sphingomyelinase activities in virulent mycobacteria)

INDEX TERM: 179734-82-8 179734-83-9
ROLE: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; biochem. and mol. anal. of phospholipase C and phospholipase D activity in mycobacteria)

INDEX TERM: 9001-87-0, Phospholipase D

ROLE: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(biochem. and mol. anal. of phospholipase C and phospholipase D activity in mycobacteria)
INDEX TERM: 9001-86-9, Phospholipase C
ROLE: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(biochem. and mol. anal. of phospholipase C and phospholipase D activity in mycobacteria)
INDEX TERM: 178195-54-5, GenBank U49511
ROLE: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; biochem. and mol. anal. of phospholipase C and phospholipase D activity in mycobacteria)
INDEX TERM: 9031-54-3, Sphingomyelinase
ROLE: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(sphingomyelinase activity in virulent mycobacteria in relation to phospholipases C and D)
OS.CITING REF COUNT: 51 THERE ARE 51 CAPLUS RECORDS THAT CITE THIS RECORD (51 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 08 Oct 2009
OS.CITING.REFS: CAPLUS 2009:1026928; 2008:1165194; 2008:355270; 2007:1205851; 2007:822937; 2006:1199109; 2006:1008155; 2006:456237; 2006:40004; 2005:1214887; 2005:1112563; 2005:943983; 2005:683843; 2005:247979; 2005:168105; 2004:442166; 2004:437638; 2004:372160; 2003:779060; 2003:759595; 2003:657350; 2002:882604; 2002:749624; 2002:576702; 2002:74414; 2001:776175; 2001:766882; 2001:706264; 2000:867853; 2000:776442; 2000:639799; 2000:603537; 2000:569478; 2000:517716; 2000:424254; 2000:340165; 2000:282598; 2000:116016; 2000:71239; 2000:16746; 1999:735504; 1999:658092; 1999:486231; 1999:363542; 1999:361072; 1999:167665; 1999:121898; 1998:616840; 1998:342194; 1998:132507
IT 9031-54-3, Sphingomyelinase
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(sphingomyelinase activity in virulent mycobacteria in relation to phospholipases C and D)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 8 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1991:136868 ZCAPLUS Full-text
DOCUMENT NUMBER: 114:136868
ORIGINAL REFERENCE NO.: 114:23097a,23100a
ENTRY DATE: Entered STN: 19 Apr 1991
TITLE: Molecular analysis of hemolytic and phospholipase C activities of Pseudomonas cepacia
AUTHOR(S): Vasil, Michael L.; Krieg, Debra P.; Kuhns, Janet S.; Ogle, John W.; Shortridge, Virginia D.; Ostroff,

Rachel M.; Vasil, Adriana I.
CORPORATE SOURCE: Health Sci. Cent., Univ. Colorado, Denver, CO, 80262, USA
SOURCE: Infection and Immunity (1990), 58(12), 4020-9
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 3-2 (Biochemical Genetics)
ABSTRACT:
By using a gene-specific fragment from the hemolytic phospholipase C (PLC) gene of P. aeruginosa as a probe and data from Southern hybridizations under reduced stringency conditions, the authors cloned a 4.2-kb restriction fragment from a beta-hemolytic P. cepacia strain which expressed hemolytic and PLC activities in Escherichia coli under the control of the lac promoter. It was found, by using a T7 phage promoter-directed expression system, that this DNA fragment carries at least two genes. One gene which shares significant DNA homol. with both PLC genes from P. aeruginosa encodes a 72-kDa protein, while the other gene encodes a 22-kDa protein. When both genes on the 4.2-kb fragment were expressed from the T7 promoter in the same cell, hemolytic and PLC activities could be detected in the cell lysate. In contrast, when each individual gene was expressed in different cells or when lysates containing the translated products of each sep. gene were mixed, neither hemolytic activity nor PLC activity would be detected. Clin. and environmental isolates of P. cepacia were examined for beta-hemolytic activity, PLC activity, sphingomyelinase activity, and reactivity in Southern hybridizations with a probe from P. cepacia which is specific for the larger gene which encodes the 72-kDa protein. There were considerable differences in the ability of the different strains to express hemolytic and PLC activities, and the results of Southern DNA-DNA hydridizations of the genomic DNAs of these strains revealed considerable differences in the probe-reactive fragments between high- and medium-stringency conditions as well as remarkable variation in size and number of probe-reactive fragments among different strains. Anal. of the genomic DNAs from hemolytic and nonhemolytic variants of an individual strain (PC-69) by agarose gel electrophoresis, Southern hybridization, and transverse alternating pulsed field gel electrophoresis suggests that the conversion of the hemolytic phenotype to the nonhemolytic phenotype is associated with either the loss of a large plasmid (>200 kb) or a large deletion of the chromosome of P. cepacia PC-69.

SUPPL. TERM: Pseudomonas hemolysin phospholipase C gene
INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(22 kDa; gene for, of Pseudomonas cepacia, phospholipase C and hemolysin in relation to)
INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(72 kDa; gene for, of Pseudomonas cepacia, phospholipase C and hemolysin in relation to)
INDEX TERM: Gene and Genetic element, microbial
(for phospholipase C and hemolysin, of Pseudomonas cepacia, mol. anal. of)
INDEX TERM: Hemolysins
(gene for, of Pseudomonas cepacia, mol. anal. of)
INDEX TERM: Plasmid and Episome
(of Pseudomonas cepacia, phospholipase C and hemolysin in relation to)
INDEX TERM: Pseudomonas cepacia
(phospholipase C and hemolysin of, genes for, mol. anal.

of)
INDEX TERM: 9001-86-9, Phospholipase C
ROLE: PRP (Properties)
(gene for, of Pseudomonas cepacia, mol. anal. of)
INDEX TERM: 9031-54-3, Sphingomyelinase
ROLE: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of Pseudomonas cepacia)
OS.CITING REF COUNT: 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (25 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 24 Apr 2009
OS.CITING.REFS: CAPLUS 2009:396736; 2008:478263; 2007:1277022; 2007:1257173; 2007:630658; 2005:1321416; 2005:1321389; 2005:166722; 2004:1056156; 2004:763122; 2004:621043; 2004:571116; 2004:15403; 2003:662571; 2002:459359; 2002:150592; 2001:433733; 2001:407502; 2000:424254; 2000:71239; 1999:765139; 1999:658092; 1999:657276; 1999:167665; 1998:296932
IT 9031-54-3, Sphingomyelinase
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of Pseudomonas cepacia)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 9 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1989:434920 ZCAPLUS Full-text
DOCUMENT NUMBER: 111:34920
ORIGINAL REFERENCE NO.: 111:5889a,5892a
ENTRY DATE: Entered STN: 05 Aug 1989
TITLE: Pseudomonas aeruginosa cytotoxin: the influence of sphingomyelin on binding and cation permeability increase in mammalian erythrocytes
AUTHOR(S): Crowell, Kathleen M.; Lutz, F.
CORPORATE SOURCE: Inst. Pharmakol. Toxikol., Justus-Liebig-Univ., Giessen, D-6300, Fed. Rep. Ger.
SOURCE: Toxicon (1989), 27(5), 531-40
CODEN: TOXIA6; ISSN: 0041-0101
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 4-5 (Toxicology)
ABSTRACT:
A cytotoxic protein isolated from P. aeruginosa damages the plasma membranes of many mammalian cells by forming pores. The binding of the 125I-labeled cytotoxin and the resulting increase of cation permeability in erythrocytes of various mammalian species was studied. The sensitivity of red blood cells was inversely related to the relative sphingomyelin content in their external surface. Thus, erythrocytes with a sphingomyelin to phosphatidylcholine ratio below 1 (dog, rat, rabbit, and man) were sensitive, whereas red blood cells with a ratio above 1 (pig, cattle, and sheep) were not attacked even with 100-fold higher cytotoxin concns. At 37° 6.8 × 103 mols. of 125I-labeled cytotoxin were bound per rabbit erythrocyte (KD = 59 mM), whereas no binding occurred to cattle cells. Cleavage of sphingomyelin by sphingomyelinase C from Bacillus cereus (EC 3.1.4.12) triggered a dose-dependent enhancement in binding and permeability increase, particularly in red blood cells with a high proportion of sphingomyelin. The KDs for all animal species investigated were 53-60 nM. Pretreatent with mainly phosphatidylcholine-hydrolyzing phospholipases D from Streptomyces chromofuscus

and cabbage (EC 3.1.4.4) of phospholipase C from Bacillus cereus (EC 3.1.4.3) did not influence the cytotoxin effect. The neg. correlation between susceptibility and the proportion of sphingomyelin in plasma membranes suggests a binding site close to sphingomyelin.

SUPPL. TERM: Pseudomonas cytotoxin sphingomyelin
INDEX TERM: Erythrocyte
(binding site of human and other mammalian, Pseudomonas aeruginosa cytotoxin binding to)
INDEX TERM: Pseudomonas aeruginosa
(cytotoxin from, binding of, to human and other mammalian erythrocyte)
INDEX TERM: Phosphatidylcholines, biological studies
Sphingomyelins
ROLE: BIOL (Biological study)
(of erythrocyte of human and other mammals, Pseudomonas aeruginosa cytotoxin binding in relation to)
INDEX TERM: Cell membrane
(of erythrocyte, sphingomyelins of, Pseudomonas aeruginosa cytotoxin binding in relation to)
INDEX TERM: Toxins
ROLE: PROC (Process)
(cyto-, of Pseudomonas aeruginosa, binding of, to human and other mammalian erythrocyte)
INDEX TERM: 9001-86-9, Phospholipase C 9001-87-0, Phospholipase D
ROLE: BIOL (Biological study)
(erythrocyte pretreatment with, Pseudomonas aeruginosa cytotoxin effect on)
INDEX TERM: 9031-54-3, Sphingomyelinase C
ROLE: BIOL (Biological study)
(erythrocyte treatment with, of human and other mammals, Pseudomonas aeruginosa binding to)
INDEX TERM: 7440-09-7, Potassium, biological studies 7440-23-5, Sodium, biological studies
ROLE: BIOL (Biological study)
(release of, by human and other mammal sphingomyelinase C-treated erythrocytes, Pseudomonas aeruginosa cytotoxin effect on)
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 16 Feb 2009
OS.CITING.REFS: CAPLUS 2003:250385; 2002:795437; 2001:720397; 2001:3231; 1999:793502; 1999:658099
IT 9031-54-3, Sphingomyelinase C
RL: BIOL (Biological study)
(erythrocyte treatment with, of human and other mammals, Pseudomonas aeruginosa binding to)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 10 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:827242 ZCAPLUS Full-text
DOCUMENT NUMBER: 151:108500
ENTRY DATE: Entered STN: 10 Jul 2009
TITLE: Pharmaceutical composition for prophylaxis and/or

symptomatic treatment of cystic fibrosis with antidepressants
INVENTOR(S): Gulbins, Erich
PATENT ASSIGNEE(S): Cycnad GmbH & Co. KG, Germany
SOURCE: PCT Int. Appl., 54pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K
CLASSIFICATION: 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 14
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009083211	A2	20090709	WO 2008-EP10996	20081222
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
DE 102007063535	A1	20090625	DE 2007-102007063535	20071221
PRIORITY APPLN. INFO.:			DE 2007-102007063535A	20071221

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2009083211	ICM	A61K
	IPCI	A61K [ICM,7]
DE 102007063535	IPCI	A61K0045-08 [I,A]; A61K0045-00 [I,C*]; A61P0043-00 [N,A]
	IPCR	A61K0045-00 [I,C]; A61K0045-08 [I,A]; A61P0043-00 [N,C]; A61P0043-00 [N,A]

ABSTRACT:
The invention relates to a pharmaceutical compound for the prophylaxis and/or symptomatic treatment of cystic fibrosis, particularly for the prophylaxis and/or treatment of infections and/or infection illnesses manifesting with cystic fibrosis, having at least one anti-depressive and preferable at least one dispersion agent and/or at least one pharmaceutically tolerated carrier material. Liquid dispersion media are used to prepare parenteral, especially inhalant
delivery systems. Thus Cftr-knockout mice and wild-type mice were treated with 4 mg amitriptyline/L water inhalant formulations; lung exts. were tested for sphingomyelinase activity and ceramide concentration

SUPPL. TERM: cystic fibrosis antidepressant inhalant
INDEX TERM: 5-HT reuptake inhibitors
Antidepressants
Burkholderia cepacia
Cystic fibrosis
Dopamine reuptake inhibitors
Haemophilus influenzae

Inhalation drug delivery systems
Lung
Noradrenaline reuptake inhibitors
Parenteral drug delivery systems
Pharmaceutical solutions
Prophylaxis
Pseudomonas aeruginosa
Staphylococcus aureus
Therapy
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)

INDEX TERM: Antibodies and Immunoglobulins
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)

INDEX TERM: 111-57-9, Ceramid 9031-54-3, Sphingomyelinase
ROLE: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)

INDEX TERM: 50-67-9, Serotonin, biological studies 51-41-2, Noradrenalin 51-61-6, Dopamine, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)

INDEX TERM: 50-47-5, Desipramine 50-48-6, Amitriptyline 50-49-7, Imipramine 58-40-2, Promazine 72-69-5, Nortriptyline 86-13-5, Benztropine 113-45-1, Methylphenidate 129-03-3, Cyproheptadine 155-09-9, Tranylcypromine 256-96-2D, 5H-Dibenz[b,f]azepine, derivative 303-49-1 303-53-7, Cyclobenzaprine 315-72-0 494-19-9, 10,11-Dihydro-5H-dibenzo[b,f]azepine 739-71-9, Trimipramine 911-45-5, Clomiphene 1668-19-5, Doxepine 4317-14-0, Amitriptyline oxide 4498-32-2, Dibenzepine 6621-47-2, Perhexiline 10262-69-8, Maprotiline 19794-93-5, Trazodon 23047-25-8, Lofepramine 24219-97-4, Mianserin 24526-64-5, Nomifensin 32359-34-5, Medifoxamine 34911-55-2, Bupropion 46817-91-8, Viloxazine 54739-18-3, Fluvoxamine 57574-09-1, Amineptine 59729-33-8, Citalopram 61869-08-7, Paroxetine 71320-77-9, Moclobemide 71620-89-8, Reboxetine 72797-41-2, Tianeptine 83366-66-9, Nefazodone 85650-52-8, Mirtazapine 92623-85-3, Milnacipran 93413-69-5, Venlafaxin 116539-59-4, Duloxetine 128196-01-0, Escitalopram
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)

IT 9031-54-3, Sphingomyelinase
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 11 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:765170 ZCAPLUS Full-text
DOCUMENT NUMBER: 151:42088
ENTRY DATE: Entered STN: 25 Jun 2009
TITLE: Pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants
PATENT ASSIGNEE(S): Cycnad G.m.b.H. & Co. K.-G., Germany
SOURCE: Ger. Offen., 12pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
CLASSIFICATION: 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 14
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102007063535	A1	20090625	DE 2007-102007063535	20071221
WO 2009083211	A2	20090709	WO 2008-EP10996	20081222

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DE 2007-102007063535A 20071221
PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 102007063535	IPCI	A61K0045-08 [I,A]; A61K0045-00 [I,C*]; A61P0043-00 [N,A]
	IPCR	A61K0045-00 [I,C]; A61K0045-08 [I,A]; A61P0043-00 [N,C]; A61P0043-00 [N,A]
WO 2009083211	IPCI	A61K [ICM,7]

ABSTRACT:
The invention concerns a pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis, in particular for prophylaxis and/or treatment of cystic fibrosis related infections and/or infectious diseases, comprising at least one antidepressant and at least one dispersion medium. Liquid dispersion media are used to prepare parenteral, especially inhalant delivery
systems. Thus Cftr-knockout mice and wild-type mice were treated with 4 mg amitriptyline/L water inhalant formulations; lung exts. were tested for sphingomyelinase activity and ceramide concentration

SUPPL. TERM: cystic fibrosis antidepressant inhalant
INDEX TERM: Antidepressants
Burkholderia cepacia
Cystic fibrosis
Haemophilus influenzae
Inhalation drug delivery systems
Lung
Parenteral drug delivery systems
Pharmaceutical solutions
Prophylaxis
Pseudomonas aeruginosa
Staphylococcus aureus
Therapy
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)
INDEX TERM: Antibodies and Immunoglobulins
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)
INDEX TERM: 480-49-9, Filipin 1400-61-9, Nystatin 7585-39-9, β-Cyclodextrin
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with; pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)
INDEX TERM: 111-57-9, Ceramid 9031-54-3, Sphingomyelinase
ROLE: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)
INDEX TERM: 50-47-5, Desipramine 50-48-6, Amitriptyline 50-49-7, Imipramine 72-69-5, Nortriptyline 256-96-2D, 5H-Dibenz[b,f]azepine, derivative 303-49-1 315-72-0 494-19-9, 10,11-Dihydro-5H-dibenzo[b,f]azepine 739-71-9, Trimipramine 1668-19-5, Doxepine 4317-14-0, Amitriptyline oxide 4498-32-2, Dibenzepine 10262-69-8, Maprotiline 23047-25-8, Lofepramine
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition for prophylaxis and/or symptomatic
treatment of cystic fibrosis with antidepressants)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD.
REFERENCE(S): (1) Anon; WO 04017949 A2
(2) Cederlund, H; Journal of Antimicobial Chemotherapy 1993, V32, PS355
(3) Hendricks, O; Inernational Journal of Antimicrobial Agents 2003, V22(3), PS262
(4) Kristiansen, J; Journal of Antimicrobial Chemotherapy 2007, V59, PS1274
(5) Munoz-Bellido, J; Interational Journal of Antimicrobial Agents 2000, V14(3), PS177
IT 9031-54-3, Sphingomyelinase

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 12 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1127533 ZCAPLUS Full-text
DOCUMENT NUMBER: 149:370531
ENTRY DATE: Entered STN: 19 Sep 2008
TITLE: Methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis
INVENTOR(S): Lu, Zhe; Ramu, Yajamana; Xu, Yanping
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 63pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
CLASSIFICATION: 1-5 (Pharmacology)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008112320	A1	20080918	WO 2008-US3507	20080317
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2007-918069P P 20070315
US 2008-64038P P 20080212

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2008112320	IPCI	A61K0038-00 [I,A]
	IPCR	A61K0038-00 [I,C]; A61K0038-00 [I,A]

ABSTRACT:
Bacterial sphingomyelinase (SMase), an ion channel modulator, suppresses immune host response. Smase is used in the treatment of cystic fibrosis, and other therapies. SMase may modulate a potassium or chloride channel in a subject: a composition comprising a therapeutically effective amount of a bacterial SMase is administered to a subject, thereby cleaving sphingomyelin. SMase may inhibit or suppress bacterial immunosuppression of a host immune system: the host is contacted with an inhibitor of the bacteria's SMase, thereby inhibiting or suppressing modulation of the host's immune cell potassium channel. An inhibitor of the bacteria's SMase may be used to treat a bacterial infection.

SUPPL. TERM: potassium chloride channel modulation bacterial

sphingomyelinase; bacterial infection treatment
sphingomyelinase inhibitor; cystic fibrosis treatment
sphingomyelinase inhibitor; T cell immunosuppression
bacteria sphingomyelinase inhibitor

INDEX TERM: Voltage-gated potassium channels
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(Kv1.3; methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)

INDEX TERM: Voltage-gated potassium channels
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(Kv2.1; methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)

INDEX TERM: Bacillus anthracis
Corynebacterium pseudotuberculosis
Pseudomonas aeruginosa
Staphylococcus aureus
(SMase of; methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)

INDEX TERM: Antibodies and Immunoglobulins
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SMase-inhibiting; methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)

INDEX TERM: T cell
(ion channels of; methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)

INDEX TERM: Anti-infective agents
Bacterial infection
Cystic fibrosis
Drug screening
Immunosuppression
(methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)

INDEX TERM: CFTR (cystic fibrosis transmembrane conductance regulator)
Chloride channels
Potassium channels
Sphingomyelins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)

INDEX TERM: Ceramides
ROLE: REM (Removal or disposal); PROC (Process)
(methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)

INDEX TERM: 1060711-19-4 1060711-20-7 1060711-28-5 1060711-30-9
1060711-32-1 1060711-35-4 1060711-38-7 1060711-41-2
1060711-43-4 1060711-45-6 1060711-46-7
ROLE: BUU (Biological use, unclassified); PRP (Properties);

BIOL (Biological study); USES (Uses)
(Loxosceles reclusa SMase peptide; methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)
INDEX TERM: 72-57-1, Trypan blue
ROLE: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)
INDEX TERM: 9031-54-3, Sphingomyelinase C
54992-31-3, Sphingomyelinase D
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)
INDEX TERM: 62-49-7, Choline 107-73-3, Phosphocholine 26993-30-6D, Sphingosine-1-phosphate, N-acyl derivs.
ROLE: REM (Removal or disposal); PROC (Process)
(methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)
INDEX TERM: 1060711-16-1 1060711-18-3 1060711-21-8 1060711-23-0
1060711-24-1 1060711-25-2 1060711-26-3
ROLE: PRP (Properties)
(unclaimed sequence; methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD.
REFERENCE(S): (1) Bursten; US 20030216414 A1 2003 ZCAPLUS
(2) Chalfant; US 20060030537 A1 2006 ZCAPLUS
(3) Liotta; US 20040039212 A1 2004 ZCAPLUS
(4) Surber; US 20030232335 A1 2003 ZCAPLUS
(5) Trotter; US 20070054894 A 2007 ZCAPLUS
IT 9031-54-3, Sphingomyelinase C
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods for modulating host ion channel function with bacterial sphingomyelinase and for treating bacterial infections and cystic fibrosis)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 13 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:789237 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:227151
ENTRY DATE: Entered STN: 10 Aug 2006
TITLE: The critical reason for production of ceramidase in Pseudomonas aeruginosa
AUTHOR(S): Okino, Nozomu
CORPORATE SOURCE: Dep. Biosci. Biotech., Grad. Sch. Bioresour. Bioenviron. Sci., Kyushu University, Fukuoka, 812-8581, Japan
SOURCE: Baiosaiensu to Indasutori (2006), 64(7), 389-390
CODEN: BIDSE6; ISSN: 0914-8981

PUBLISHER: Baioindasutori Kyokai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
CLASSIFICATION: 10-0 (Microbial, Algal, and Fungal Biochemistry)
ABSTRACT:
A review on the simultaneous induction of ceramidase and sphingomyelinase by lipids in P. aeruginosa, and augmentation of sphingomyelinase-induced hemolysis by ceramidase.

SUPPL. TERM: review Pseudomonas ceramidase sphingomyelinase hemolysis
INDEX TERM: Hemolysis
Pseudomonas aeruginosa
(role of ceramidase in hemolysis induced by sphingomyelinase of Pseudomonas aeruginosa)
INDEX TERM: 9031-54-3, Sphingomyelinase
56467-83-5, Ceramidase
ROLE: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(role of ceramidase in hemolysis induced by sphingomyelinase of Pseudomonas aeruginosa)
IT 9031-54-3, Sphingomyelinase
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(role of ceramidase in hemolysis induced by sphingomyelinase of Pseudomonas aeruginosa)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 14 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:171714 ZCAPLUS Full-text
DOCUMENT NUMBER: 136:210564
ENTRY DATE: Entered STN: 08 Mar 2002
TITLE: Detecting and influencing the expression or function of CD95/CD95L in infections
INVENTOR(S): Lang, Florian; Gulbins, Erich
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K038-00
CLASSIFICATION: 1-7 (Pharmacology)
Section cross-reference(s): 9, 15
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017950	A2	20020307	WO 2001-EP9889	20010828

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10042853	A1	20020425	DE 2000-10042853			20000830
AU 2002012170	A	20020313	AU 2002-12170			20010828
PRIORITY APPLN. INFO.:			DE 2000-10042853	A		20000830
			WO 2001-EP9889	W		20010828

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002017950	ICM	A61K038-00
	IPCI	A61K0038-00 [ICM,7]
	IPCR	A61K0038-17 [I,C*]; A61K0038-17 [I,A]
	ECLA	A61K038/17A2
DE 10042853	IPCI	A61K0038-17 [ICM,7]; C12Q0001-68 [ICS,7]
	IPCR	A61K0038-17 [I,C*]; A61K0038-17 [I,A]
	ECLA	A61K038/17A2
AU 2002012170	IPCI	A61K0038-00 [ICM,7]
	IPCR	A61K0038-17 [I,C*]; A61K0038-17 [I,A]
	ECLA	A61K038/17A2

ABSTRACT:
The invention discloses the use of a substance for detecting CD95 and/or CD95L, or members of the signal transduction cascade of CD95 and/or CD95L, in order to identify susceptibility to diseases that are related to an infection. The invention also discloses the use of an active substance for preventing and treating infections, in particular, bacterial infections, in which the active substance influences the expression and/or function of CD95 and/or CD95L, or members of the signal transduction cascade of CD95 and/or CD95L, thereby inducing apoptosis in the infected cells.

SUPPL. TERM: CD95 detection modulation infection treatment diagnosis apoptosis; CD95L detection modulation infection treatment diagnosis apoptosis

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CAD; CD95/CD95L detection and modulation in infections)

INDEX TERM: Anti-infective agents
Antibacterial agents
Apoptosis
Diagnosis
Drug delivery systems
Fibroblast
Human
Infection
Lymphocyte
Pseudomonadaceae
Pseudomonas aeruginosa
Sepsis
Signal transduction, biological
Test kits
Transplant and Transplantation
(CD95/CD95L detection and modulation in infections)

INDEX TERM: CFTR (cystic fibrosis transmembrane conductance regulator)
Fas antigen
Fas ligand
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CD95/CD95L detection and modulation in infections)

INDEX TERM: Peptides, biological studies
Polynucleotides
Proteins
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD95/CD95L detection and modulation in infections)

INDEX TERM: Animal cell line
(Chang; CD95/CD95L detection and modulation in infections)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(FADD; CD95/CD95L detection and modulation in infections)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GADD 153; CD95/CD95L detection and modulation in infections)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(I-CAD; CD95/CD95L detection and modulation in infections)

INDEX TERM: Transcription factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(NF-κB (nuclear factor of κ light chain gene enhancer in B-cells); CD95/CD95L detection and modulation in infections)

INDEX TERM: Infection
(bacterial; CD95/CD95L detection and modulation in infections)

INDEX TERM: Epithelium
(bronchial; CD95/CD95L detection and modulation in infections)

INDEX TERM: Bone marrow
(cell; CD95/CD95L detection and modulation in infections)

INDEX TERM: Eye
(conjunctiva, epithelium; CD95/CD95L detection and modulation in infections)

INDEX TERM: Epithelium
(conjunctival; CD95/CD95L detection and modulation in infections)

INDEX TERM: Bronchi
Lung
(epithelium; CD95/CD95L detection and modulation in infections)

INDEX TERM: Drug delivery systems
(inhalants; CD95/CD95L detection and modulation in infections)

INDEX TERM: Drug delivery systems
(injections, i.v.; CD95/CD95L detection and modulation in infections)

INDEX TERM: Drug delivery systems
(oral; CD95/CD95L detection and modulation in infections)

INDEX TERM: Epithelium
(pulmonary; CD95/CD95L detection and modulation in infections)

INDEX TERM: Drug delivery systems
(topical; CD95/CD95L detection and modulation in

infections)
INDEX TERM: Niemann-Pick disease
(type A; CD95/CD95L detection and modulation in infections)
INDEX TERM: 9001-84-7, Phospholipase A2 9031-54-3, Sphingomyelinase 155215-87-5, Jnk kinase 169592-56-7, Caspase 3 179241-78-2, Caspase 8
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(CD95/CD95L detection and modulation in infections)
IT 9031-54-3, Sphingomyelinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD95/CD95L detection and modulation in infections)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 15 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:887890 ZCAPLUS Full-text
DOCUMENT NUMBER: 136:163998
ENTRY DATE: Entered STN: 09 Dec 2001
TITLE: Chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus
AUTHOR(S): Uchida, Ryuji; Tomoda, Hiroshi; Arai, Masayoshi; Omura, Satoshi
CORPORATE SOURCE: Kitasato Institute for Life Sciences, Kitasato University and The Kitasato Institute, Tokyo, 108-8641, Japan
SOURCE: Journal of Antibiotics (2001), 54(11), 882-889
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 10-5 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 16

ABSTRACT:
Chlorogentisylquinone, a new inhibitor of neutral sphingomyelinase activity, was purified from the culture broth of a fungal strain FOM-8108 isolated from a marine environment by solvent extraction, silica gel chromatog. and Sephadex LH-20 chromatog. Its chemical structure was elucidated by spectroscopic studies including 1H, 13C, DEPT, HMQC and HMBC NMR expts. Chlorogentisylquinone inhibited neutral sphingomyelinase activity of rat brain membranes with an IC50 value of 1.2 μM.

SUPPL. TERM: chlorogentisylquinone sphingomyelinase inhibitor marine fungus
INDEX TERM: Liquid chromatography
(adsorption; chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus)
INDEX TERM: New natural products
(chlorogentisylquinone (quinone))
INDEX TERM: Antibiotic resistance
Antibiotics
Antitumor agents
Cytotoxicity
Extraction
Fermentation

Ion exchange liquid chromatography
(chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus)
INDEX TERM: Fungi
(marine, FOM-8108; chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus)
INDEX TERM: Molecular structure, natural product
(of chlorogentisylquinone)
INDEX TERM: Acholeplasma laidlawii
Aspergillus niger
Bacillus subtilis
Bacteroides fragilis
Candida albicans
Escherichia coli
Micrococcus luteus
Mucor racemosus
Mycobacterium smegmatis
Pseudomonas aeruginosa
Pyricularia oryzae
Saccharomyces cerevisiae
Staphylococcus aureus
Xanthomonas oryzae
(target microorganism; chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus)
INDEX TERM: 644-17-7P, Gentisylquinone
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus)
INDEX TERM: 333344-08-4P, Chlorogentisylquinone
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus)
INDEX TERM: 106-51-4, 1,4-Benzoquinone, biological studies 695-99-8, 2-Chloro-1,4-benzoquinone 873-63-2, 3-Chlorobenzyl alcohol 9031-54-3, Neutral sphingomyelinase
33524-31-1, 2,5-Dimethoxybenzyl alcohol
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus)
OS.CITING REF COUNT: 28 THERE ARE 28 CAPLUS RECORDS THAT CITE THIS RECORD (28 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 16 Feb 2009
OS.CITING.REFS: CAPLUS 2008:1469774; 2008:1322877; 2008:16023; 2007:923970; 2007:599015; 2007:353824; 2007:333917; 2006:1297522; 2006:450838; 2006:127266; 2006:81597; 2006:34; 2005:510603; 2005:500403; 2005:376939; 2005:45858; 2004:1018190; 2004:678927; 2004:676227; 2004:303197; 2004:251371; 2004:98515; 2003:912051; 2003:246612; 2002:941198; 2002:807064; 2002:708532; 2002:537898
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

RECORD.

REFERENCE(S): (1) Dobrowsky, R; J Biol Chem 1992, V267, P5048 ZCAPLUS
(2) Engle, B; Helv Chem Acta 1947, V30, P1472
(3) Hannun, Y; J Biol Chem 1994, V269, P3125 ZCAPLUS
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IT 9031-54-3, Neutral sphingomyelinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chlorogentisylquinone, a new neutral sphingomyelinase inhibitor, produced by a marine fungus)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 16 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1999:60878 ZCAPLUS Full-text
DOCUMENT NUMBER: 130:280210
ENTRY DATE: Entered STN: 29 Jan 1999
TITLE: Ceramidase activity in bacterial skin flora as a possible cause of ceramide deficiency in atopic dermatitis
AUTHOR(S): Ohnishi, Yoshinori; Okino, Nozomu; Ito, Makoto; Imayama, Shuhei
CORPORATE SOURCE: Department of Dermatology, Faculty of Medicine, Kyushu University, Fukuoka, Japan
SOURCE: Clinical and Diagnostic Laboratory Immunology (1999), 6(1), 101-104
CODEN: CDIMEN; ISSN: 1071-412X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 14-9 (Mammalian Pathological Biochemistry)
ABSTRACT:
A marked decrease in the content of ceramide has been reported in the horny layer of the epidermis in atopic dermatitis (AD). This decrease impairs the permeability barrier of the epidermis, resulting in the characteristic dry and easily antigen-permeable skin of AD, since ceramide serves as the major water-holding mol. in the extracellular space of the horny layer. On the other hand, the skin of such patients is frequently colonized by bacteria, most typically by Staphylococcus aureus, possessing genes such as those for sphingomyelinase, which are related to sphingolipid metabolism We therefore tried to identify a possible correlation between the ceramide content and the

bacterial flora obtained from the skin of 25 patients with AD vs. that of 24 healthy subjects, using a thin-layer chromatog. assay of the sphingomyelin-associated enzyme activities secreted from the bacteria. The findings of the assay demonstrated that ceramidase, which breaks ceramide down into sphingosine and fatty acid, was secreted significantly more from the bacterial flora obtained from both the lesional and the nonlesional skin of patients with AD than from the skin of healthy subjects; sphingomyelinase, which breaks sphingomyelin down into ceramide and phosphorylcholine, was secreted from the bacterial flora obtained from all types of skin at similar levels for the patients with AD and the healthy controls. The finding that the skin of patients with AD is colonized by ceramidase-secreting bacteria thus suggests that microorganisms are related to the deficiency of ceramide in the horny layer of the epidermis, which increases the hypersensitivity of skin in AD patients by impairing the permeability barrier.

SUPPL. TERM: ceramidase bacteria ceramide deficiency atopic dermatitis
INDEX TERM: Dermatitis
(atopic; ceramidase-secreting bacteria as possible cause of ceramide deficiency in atopic dermatitis in human)
INDEX TERM: Bacteria (Eubacteria)
Pseudomonas aeruginosa
Psoriasis
Staphylococcus aureus
(ceramidase-secreting bacteria as possible cause of ceramide deficiency in atopic dermatitis in human)
INDEX TERM: Disease, animal
(deficiency, ceramide deficiency; ceramidase-secreting bacteria as possible cause of ceramide deficiency in atopic dermatitis in human)
INDEX TERM: Ceramides
ROLE: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(deficiency; ceramidase-secreting bacteria as possible cause of ceramide deficiency in atopic dermatitis in human)
INDEX TERM: Skin
(epidermis; ceramidase-secreting bacteria as possible cause of ceramide deficiency in atopic dermatitis in human)
INDEX TERM: 56467-83-5, Ceramidase
ROLE: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(ceramidase-secreting bacteria as possible cause of ceramide deficiency in atopic dermatitis in human)
INDEX TERM: 9031-54-3, Sphingomyelinase
ROLE: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ceramidase-secreting bacteria as possible cause of ceramide deficiency in atopic dermatitis in human)
OS.CITING REF COUNT: 37 THERE ARE 37 CAPLUS RECORDS THAT CITE THIS RECORD (37 CITINGS)
DATE LAST CITED: Date last citing reference entered STN: 23 Sep 2009
OS.CITING.REFS: CAPLUS 2009:669062; 2009:510948; 2009:604067; 2009:520371; 2009:372586; 2009:513242; 2008:1456682; 2008:921223; 2007:1418703; 2007:977423; 2007:676913; 2007:676909; 2007:676898; 2007:15526; 2006:1126992; 2006:1020005; 2006:484304; 2006:139667; 2005:1110135; 2005:1036791;

2005:391973; 2005:339731; 2005:321527; 2005:42379; 2004:174177; 2004:2248; 2003:563650; 2003:484424; 2003:199977; 2002:817770; 2002:809352; 2002:712410; 2002:646676; 2000:734151; 2000:364478; 2000:270269; 1999:457772

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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IT 9031-54-3, Sphingomyelinase
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(ceramidase-secreting bacteria as possible cause of ceramide deficiency in atopic dermatitis in human)

RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 17 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:502775 ZCAPLUS Full-text
DOCUMENT NUMBER: 129:120818
ORIGINAL REFERENCE NO.: 129:24725a
ENTRY DATE: Entered STN: 13 Aug 1998
TITLE: Bacterial ceramidase involved in atopic dermatitis
AUTHOR(S): Okino, Nozomu; Ito, Makoto
CORPORATE SOURCE: Fac. Agric., Kyushu Univ., Fukuoka, 812, Japan
SOURCE: Kagaku to Seibutsu (1998), 36(8), 484-486
CODEN: KASEAA; ISSN: 0453-073X
PUBLISHER: Gakkai Shuppan Senta
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

CLASSIFICATION: 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 10

ABSTRACT:
A review with 14 refs. on isolation of Pseudomonas aeruginosa and other bacteria producing sphingolipid ceramide N-deacylase, sphingomyelinase, or ceramidase from patients with atopic dermatitis, structure of the ceramidase of P. aeruginosa, activity of the bacterial enzymes, and possible disturbance of human keratinocyte differentiation by infection of the bacteria.

SUPPL. TERM: review bacterial ceramidase atopic dermatitis
INDEX TERM: Dermatitis
(atopic; bacterial ceramidase involved in atopic dermatitis)
INDEX TERM: Bacteria (Eubacteria)
(bacterial ceramidase involved in atopic dermatitis)
INDEX TERM: 56467-83-5, Ceramidase
ROLE: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(bacterial ceramidase involved in atopic dermatitis)

L115 ANSWER 18 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:487851 ZCAPLUS Full-text
DOCUMENT NUMBER: 109:87851
ORIGINAL REFERENCE NO.: 109:14563a,14566a
ENTRY DATE: Entered STN: 17 Sep 1988
TITLE: The role of lipids in the action of Pseudomonas aeruginosa cytotoxin on mammalian cells
AUTHOR(S): Lutz, F.; Crowell, K.; Lewicki, N.; Conrath, R.
CORPORATE SOURCE: Inst. Pharmakol. Toxikol., Justus-Liebig-Univ., Giessen, D-6300, Fed. Rep. Ger.
SOURCE: Zentralblatt fuer Bakteriologie, Mikrobiologie und Hygiene, Abteilung 1, Supplemente (1988), 17(Bact. Protein Toxins), 95-102
CODEN: ZBMSDR; ISSN: 0172-5629
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 4-5 (Toxicology)
ABSTRACT:
The amount of P. aeruginosa cytotoxin bound specifically to erythrocytes of various species correlates with their toxin-response and is inversely related to the sphingomyelin content of the membrane. Treatment of erythrocytes with sphingomyelinase C from Bacillus cereus increases binding capacity and toxin response, whereas the toxin-membrane dissociation constant remains unchanged. The temperature shift between 21° and 30° in the cytotoxin-induced permeability increase was not influenced by alteration of fatty acid composition of Ehrlich ascites tumor cells by fat diet to the tumor-bearing mice. Apparently, sphingomyelin mols., located close to toxin acceptors, interfere with cytotoxin binding.

SUPPL. TERM: Pseudomonas cytotoxin binding membrane sphingomyelin
INDEX TERM: Pseudomonas aeruginosa
(cytotoxin of, binding of, to cell membrane, sphingomyelin effect on)
INDEX TERM: Sphingomyelins
ROLE: BIOL (Biological study)
(Pseudomonas aeruginosa cytotoxin binding to erythrocyte in relation to)
INDEX TERM: Cell membrane

(Pseudomonas aeruginosa cytotoxin
binding to, sphingomyelin in relation to)
INDEX TERM: Erythrocyte
(Pseudomonas aeruginosa cytotoxin
binding to, sphingomyelins effect on)
INDEX TERM: Fatty acids, biological studies
ROLE: BIOL (Biological study)
(Pseudomonas aeruginosa cytotoxin
toxicity to Ehrlich ascites cells in relation to)
INDEX TERM: Animal cell line
(Ehrlich ascites, Pseudomonas
aeruginosa cytotoxin toxicity to, fatty acids in
relation to)
INDEX TERM: Toxins
ROLE: BIOL (Biological study)
(cyto-, of Pseudomonas aeruginosa,
binding of, to cell membrane, sphingomyelins effect on)

L115 ANSWER 19 OF 27 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:128235 ZCAPLUS Full-text
DOCUMENT NUMBER: 104:128235
ORIGINAL REFERENCE NO.: 104:20287a,20290a
ENTRY DATE: Entered STN: 19 Apr 1986
TITLE: Manufacture of sphingomyelinase with Bacillus cereus
INVENTOR(S): Ando, Noboru; Oishi, Michio
PATENT ASSIGNEE(S): Chiyoda Chemical Engineering and Construction Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
INT. PATENT CLASSIF.:
MAIN: C12N009-16
INDEX: C12N009-16, C12R001-085
CLASSIFICATION: 16-4 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 7
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60221084	A	19851105	JP 1984-76585	19840418
JP 62047515	B	19871008		

PRIORITY APPLN. INFO.: JP 1984-76585 19840418
PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 60221084	ICM	C12N009-16
	ICI	C12N009-16, C12R001-085
	IPCI	C12N0009-16 [ICM,4]; C12N0009-16 [ICI,4]; C12R0001-085 [ICI,4]
	IPCR	C12N0009-16 [I,C*]; C12N0009-16 [I,A]; C12R0001-085 [N,A]; C12R0001-38 [N,A]

ABSTRACT:
Sphingomyelinase is produced with a culture of B. cereus in the presence of Pseudomonas species. Thus, B. cereus and Pseudomonas T-1 were aerobically cultivated in a medium containing peptone 2, yeast extract 1, glycerin 2, NaCl 1, and
MgSO4 0.5% (pH 7.5) at 30° for 8 h. The culture filtrate was treated with 70% saturated (NH4)2SO4 and subjected to chromatog. on a series of columns

(Sephadex G50, DEAE cellulose, PBE94 gel, Toyopearl HW 55f) to obtain a preparation with 1500-fold purification

SUPPL. TERM: sphingomyelinase prodn Bacillus fermn
INDEX TERM: Pseudomonas
Pseudomonas aeruginosa
Pseudomonas fluorescens
Pseudomonas putida
Pseudomonas schuylkilliensis
Pseudomonas stutzeri
(sphingomyelinase manufacture with Bacillus cereus in presence of)
INDEX TERM: Bacillus cereus
(sphingomyelinase manufacture with, in Pseudomonas presence)
INDEX TERM: Fermentation
(sphingomyelinase, with Bacillus cereus in Pseudomonas presence)
INDEX TERM: 9031-54-3P
ROLE: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, with Bacillus cereus, in Pseudomonas presence)
IT 9031-54-3P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, with Bacillus cereus, in Pseudomonas presence)
RN 9031-54-3 ZCAPLUS
CN Sphingomyelinase C (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L115 ANSWER 20 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2006123415 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16464252
TITLE: Acceleration of epithelial cell syndecan-1 shedding by anthrax hemolytic virulence factors.
AUTHOR: Popova Taissia G; Millis Bryan; Bradburne Chris; Nazarenko Svetlana; Bailey Charles; Chandhoke Vikas; Popov Serguei G
CORPORATE SOURCE: National Center for Biodefense and Infectious Diseases, George Mason University, Manassas, VA 20110, USA.. tpopova@gmu.edu
SOURCE: BMC microbiology, (2006) Vol. 6, pp. 8. Electronic Publication: 2006-02-07.
Journal code: 100966981. E-ISSN: 1471-2180.
Report No.: NLM-PMC1386683.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200612
ENTRY DATE: Entered STN: 3 Mar 2006
Last Updated on STN: 19 Dec 2006
Entered Medline: 14 Dec 2006
ABSTRACT:
BACKGROUND: It has been recently reported that major pathogens Staphylococcus

aureus and Pseudomonas aeruginosa accelerate a normal process of cell surface syndecan-1 (Syndl) ectodomain shedding as a mechanism of host damage due to the production of shedding-inducing virulence factors. We tested if acceleration of Syndl shedding takes place in vitro upon treatment of epithelial cells with B. anthracis hemolysins, as well as in vivo during anthrax infection in mice. RESULTS: The isolated anthrax hemolytic proteins AnlB (sphingomyelinase) and AnlO (cholesterol-binding pore-forming factor), as well as ClnA (B. cereus homolog of B. anthracis phosphatidyl choline-preferring phospholipase C) cause accelerated shedding of Syndl and E-cadherin from epithelial cells and compromise epithelial barrier integrity within a few hours. In comparison with hemolysins in a similar range of concentrations, anthrax lethal toxin (LT) also accelerates shedding albeit at slower rate. Individual components of LT, lethal factor and protective antigen are inactive with regard to shedding. Inhibition experiments favor a hypothesis that activities of tested bacterial shedding inducers converge on the stimulation of cytoplasmic tyrosine kinases of the Syk family, ultimately leading to activation of cellular sheddase. Both LT and AnlO modulate ERK1/2 and p38 MAPK signaling pathways, while JNK pathway seems to be irrelevant to accelerated shedding. Accelerated shedding of Syndl also takes place in DBA/2 mice challenged with Bacillus anthracis (Sterne) spores. Elevated levels of shed ectodomain are readily detectable in circulation after 24 h. CONCLUSION: The concerted acceleration of shedding by several virulence factors could represent a new pathogenic mechanism contributing to disruption of epithelial or endothelial integrity, hemorrhage, edema and abnormal cell signaling during anthrax infection.

CONTROLLED TERM: Animals
Antigens, Bacterial: ME, metabolism
*Bacillus anthracis: ME, metabolism
Bacterial Toxins: ME, metabolism
Cadherins: ME, metabolism
Cell Line
*Epithelial Cells: MI, microbiology
*Epithelial Cells: SE, secretion
Hemolysin Proteins: ME, metabolism
Humans
L-Lactate Dehydrogenase: ME, metabolism
Mice
Mice, Inbred DBA
Sphingomyelin Phosphodiesterase: ME, metabolism
*Syndecan-1: SE, secretion
Type C Phospholipases: ME, metabolism
*Virulence Factors: ME, metabolism

CHEMICAL NAME: 0 (Antigens, Bacterial); 0 (Bacterial Toxins); 0 (Cadherins); 0 (Hemolysin Proteins); 0 (Syndecan-1); 0 (Virulence Factors); 0 (anthrax toxin); EC 1.1.1.27 (L-Lactate Dehydrogenase); EC 3.1.4.- (Type C Phospholipases); EC 3.1.4.12 (Sphingomyelin Phosphodiesterase); EC 3.1.4.3 (phosphatidylcholine-specific phospholipase C)

L115 ANSWER 21 OF 27 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1993170110 EMBASE Full-text
TITLE: Bacterial phospholipases C.
AUTHOR: Titball, R.W. (correspondence)
CORPORATE SOURCE: Chem./Biol. Defence Establishment, Porton Down, Salisbury SP4 0JQ, United Kingdom.
SOURCE: Microbiological Reviews, (1993) Vol. 57, No. 2, pp. 347-366.
ISSN: 0146-0749 CODEN: MBRED3

COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 1993
Last Updated on STN: 11 Jul 1993

ABSTRACT: A variety of pathogenic bacteria produce phospholipases C, and since the discovery in 1944 that a bacterial toxin (Clostridium perfringens alpha-toxin) possessed an enzymatic activity, there has been considerable interest in this class of proteins. Initial speculation that all phospholipases C would have lethal properties has not been substantiated. Most of the characterized enzymes fall into one of four groups of structurally related proteins: the zinc-metallophospholipases C, the sphingomyelinases, the phosphatidylinositol-hydrolyzing enzymes, and the pseudomonad phospholipases C. The zinc-metallophospholipases C have been most intensively studied, and lethal toxins within this group possess an additional domain. The toxic phospholipases C can interact with eukaryotic cell membranes and hydrolyze phosphatidylcholine and sphingomyelin, leading to cell lysis. However, measurement of the cytolytic potential or lethality of phospholipases C may not accurately indicate their roles in the pathogenesis of disease. Subcytolytic concentrations of phospholipase C can perturb host cells by activating the arachidonic acid cascade or protein kinase C. Nonlethal phospholipases C, such as the Listeria monocytogenes PLC-A, appear to enhance the release of the organism from the host cell phagosome. Since some phospholipases C play important roles in the pathogenesis of disease, they could form components of vaccines. A greater understanding of the modes of action and structure-function relationships of phospholipases C will facilitate the interpretation of studies in which these enzymes are used as membrane probes and will enhance the use of these proteins as models for eukaryotic phospholipases C.

CONTROLLED TERM: Medical Descriptors:
bacterial membrane
clostridium perfringens
cytotoxicity
enzyme activation
enzyme assay
enzyme mechanism
enzyme purification
enzyme synthesis
gene expression regulation
*gram negative bacterium
*gram positive bacterium
legionella
listeria monocytogenes
nonhuman
priority journal
pseudomonas aeruginosa
review
staphylococcus aureus
CONTROLLED TERM: Drug Descriptors:
arachidonic acid
clostridium toxin: EC, endogenous compound
immunotoxin
metalloprotein: EC, endogenous compound
phosphatidylinositol: EC, endogenous compound
*phospholipase c: EC, endogenous compound
sphingomyelin phosphodiesterase: EC, endogenous compound

staphylococcus toxin: EC, endogenous compound
vaccine
zinc: EC, endogenous compound
CAS REGISTRY NO.: (arachidonic acid) 506-32-1, 6610-25-9, 7771-44-0; (phospholipase C) 9001-86-9; (sphingomyelin phosphodiesterase) 9031-54-3; (zinc) 7440-66-6

L115 ANSWER 22 OF 27 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:634904 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600624932
TITLE: Sphingolipid-binding proteins.
AUTHOR(S): Snook, C. F.; Jones, J. A.; Hannun, Y. A. [Reprint Author]
CORPORATE SOURCE: Med Univ S Carolina, Dept Biochem and Mol Biol, 173 Ashley Ave,POB 25059,Room 501A, Charleston, SC 29425 USA
snookc@musc.edu; hannun@musc.edu
SOURCE: Biochimica et Biophysica Acta, (AUG 2006) Vol. 1761, No. 8, pp. 927-946.
ISSN: 1388-1981.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Nov 2006
Last Updated on STN: 22 Nov 2006
ABSTRACT:Emerging information on sphingolipid metabolism and signaling is leading to a better understanding of cellular processes such as apoptosis, cancer, cell survival and aging. In this review, we discuss the involvement of sphingolipids in these processes and focus on underlying mechanisms based on sphingolipid:protein interactions. Due to the inherent difficulty of studying lipids, we discuss techniques that are useful in the elucidation of these interactions. We classify sphingolipid-binding proteins into four main classes: receptor, effector, enzyme, and transporter. Known structures of sphingolipid-binding proteins are surveyed, and sphingolipid-binding characteristics are described, acknowledging the limitations that there are presently insufficient protein: sphingolipid complexes for more definitive conclusions on this topic. Finally we summarize relevant literature to better inform the reader about sphingolipid:protein interactions. (c) 2006 Elsevier B.V. All rights reserved.

sphingomyelin; glycosphingolipid; GM2 activator protein; ceramide 1-phosphate; sulfatide; ceramidase [EC 3.5.1.23]; sphingosine kinase; sphingomyelinase; CERT; sphingolipid: metabolism, signaling; sphingolipid-binding protein

INDEX TERMS: Miscellaneous Descriptors
cell apoptosis; sphingolipid-protein interaction

ORGANISM: Classifier
Arachnida 75402
Super Taxa
Chelicerata; Arthropoda; Invertebrata; Animalia
Organism Name
Loxosceles leata (species)
Sicarius (genus)
Taxa Notes
Animals, Arthropods, Chelicerates, Invertebrates

ORGANISM: Classifier
Ascomycetes 15100
Super Taxa
Fungi; Plantae
Organism Name
Saccharomyces cerevisiae (species) [yeast (common)]
Taxa Notes
Fungi, Microorganisms, Nonvascular Plants, Plants

ORGANISM: Classifier
Cruciferae 25880
Super Taxa
Dicotyledones; Angiospermae; Spermatophyta; Plantae
Organism Name
Arabidopsis thaliana (species)
Taxa Notes
Angiosperms, Dicots, Plants, Spermatophytes, Vascular Plants

ORGANISM: Classifier
Endospore-forming Gram-Positives 07810
Super Taxa
Eubacteria; Bacteria; Microorganisms
Organism Name
Clostridium botulinum (species)
Bacillus cereus (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier
Enterobacteriaceae 06702
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Escherichia coli (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier
Lepidoptera 75330
Super Taxa
Insecta; Arthropoda; Invertebrata; Animalia
Organism Name
Sphinx (genus)
Taxa Notes
Animals, Arthropods, Insects, Invertebrates
ORGANISM: Classifier
Lichenes 19000
Super Taxa
Plantae
Organism Name
Podospora anserina (species)
Taxa Notes
Nonvascular Plants, Plants
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
ORGANISM: Classifier
Nematoda 51300
Super Taxa
Aschelminthes; Helminthes; Invertebrata; Animalia
Organism Name
Caenorhabditis elegans (species)
Taxa Notes
Animals, Aschelminths, Helminths, Invertebrates
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGANISM: Classifier
Regular Nonsporing Gram-Positive Rods 07830
Super Taxa
Eubacteria; Bacteria; Microorganisms
Organism Name
Listeria ivanovii (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms
REGISTRY NUMBER: 104404-17-3 (ceramide)
26993-30-6 (sphingosine 1-phosphate)
56467-83-5 (ceramidase)
56467-83-5 (EC 3.5.1.23)
50864-48-7 (sphingosine kinase)
9031-54-3 (sphingomyelinase)

L115 ANSWER 23 OF 27 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:335349 BIOSIS Full-text

DOCUMENT NUMBER: PREV200700323350
TITLE: Selective toxicity suggests receptor mediated uptake of the hemolytic phospholipase C of ~~Pseudomonas aeruginosa~~.
AUTHOR(S): Stonehouse, M. J. [Reprint Author]; Wadsworth, S. J.; Goldfine, H.; Vasil, A.; Vasil, M. L.
CORPORATE SOURCE: Univ Colorado, Hlth Sci Ctr, Denver, CO USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2004) Vol. 104, pp. 89.
Meeting Info.: 104th General Meeting of the American-Society-for-Microbiology. New Orleans, LA, USA. May 23 -27, 2004. Amer Soc Microbiol.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 May 2007
Last Updated on STN: 30 May 2007
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Cytology - Human 02508
Enzymes - General and comparative studies: coenzymes 10802
Toxicology - General and methods 22501
Physiology and biochemistry of bacteria 31000
Medical and clinical microbiology - Bacteriology 36002
INDEX TERMS: Major Concepts
Toxicology; Infection; Enzymology (Biochemistry and Molecular Biophysics)
INDEX TERMS: Diseases
~~Pseudomonas aeruginosa~~ infection: bacterial disease, etiology
INDEX TERMS: Chemicals & Biochemicals
~~sphingomyelinase~~ [EC 3.1.4.12]; phospholipase C [EC 3.1.4.3]; arginine-glycine-aspartate; integrin antibody
INDEX TERMS: Miscellaneous Descriptors
selective toxicity
ORGANISM: Classifier
Cricetidae 86310
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
CHO cell line (cell_line): Chinese hamster ovary cells
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
ORGANISM: Classifier
Endospore-forming Gram-Positives 07810
Super Taxa
Eubacteria; Bacteria; Microorganisms
Organism Name
Bacillus cereus (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGANISM: Classifier
Gram-Negative Aerobic Rods and Cocci 06500
Super Taxa
Eubacteria; Bacteria; Microorganisms
Organism Name
Francisella rularensis (species): pathogen

Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HUVEC cell line (cell_line): human umbilical vein endothelial cells
HeLa cell line (cell_line): human cervical cancer cells
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
L929 cell line (cell_line): murine fibrosarcoma cells
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species): pathogen
Burkholderia pseudomallei (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
REGISTRY NUMBER: 9031-54-3 (sphingomyelinase)
9031-54-3 (EC 3.1.4.12)
63551-76-8 (phospholipase C)
63551-76-8 (EC 3.1.4.3)

L115 ANSWER 24 OF 27 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:517187 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300519809
TITLE: Selective toxicity suggests receptor mediated uptake of the hemolytic phospholipase C of Pseudomonas aeruginosa.
AUTHOR(S): Stonehouse, M. J. [Reprint Author]; Wadsworth, S. J.; Vasil, A. [Reprint Author]; Vasil, M. L. [Reprint Author]
CORPORATE SOURCE: Univ. of Colorado Health Science Center, Denver, CO, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-055. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom. Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003
ABSTRACT:Phosphatidylcholine preferring phospholipases C (PC-PLC) and sphingomyelinases (SMases) have been associated with a growing number of

critical signal transduction mechanisms in eukaryotic cells. While the evidence for mammalian SMases is clear, the existence of mammalian PC-PLCs is controversial. The studies demonstrating PC-PLC activity in mammalian cells have relied on detection of elevated diacylglycerol (DAG) levels and inhibition by the putative, specific PC-PLC competitive inhibitor, D609. This lack of structural and mechanistic information for mammalian PC-PLC has accorded prokaryotic PC-PLC added significance. Recently, we reported the 1500 fold purification and characterization of the hemolytic phospholipase C (PLC) of Pseudomonas aeruginosa (PlcHR2), the paradigm for a novel class of PLC/phosphatase that have been identified in a number of microbial pathogens including Mycobacterium tuberculosis, Francisella tularensis, and Burkholderia pseudomallei. The members of this class of PC-PLC do not share any amino acid homology with the well-characterized Bacillus cereus PC-PLC. In this current study we set out to examine the effect of PlcHR2 on eukaryotic cells. Addition of PlcHR2 onto different eukaryotic cell lines resulted in varying levels of cytotoxicity. Both HUVEC and CHO are extremely sensitive to PlcHR2 while HeLa, L929, and primary human lung epithelial cells are relatively resistant to PlcHR2. Furthermore, purified PlcHR2 induces release of intracellular calcium from HUVEC. These data suggest the possibility of a toxin like receptor-mediated interaction. PlcH contains an arginine-glycine-aspartate (RGD) motif and RGD motifs are involved in integrin binding. It is possible that PlcH is interacting with integrins on cell surfaces of certain cell through its RGD motif rendering these cells more susceptible to PlcHR2. Preliminary data that supports this hypothesis is that in-vitro PlcHR2 binds integrin alphaIIbbeta3 and RGD peptides block PlcHR2 induced release of intracellular calcium in HUVECs. Studies with biotinylated PlcHR2 are underway to further investigate this receptor-mediated interaction.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - General 02502
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Minerals 10069
Enzymes - General and comparative studies: coenzymes 10802
Respiratory system - Physiology and biochemistry 16004
Toxicology - General and methods 22501
Morphology and cytology of bacteria 30500
Physiology and biochemistry of bacteria 31000

INDEX TERMS: Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Infection; Toxicology

INDEX TERMS: Parts, Structures, & Systems of Organisms
lung epithelial cells: respiratory system

INDEX TERMS: Chemicals & Biochemicals
calcium; integrin alpha-IIb-beta-3; phospholipase C H [PlcH]: arginine-glycine-aspartate motif; phospholipase C HR-2 [PlcHR-2]: biotinylated, hemolytic, receptor mediated uptake, cytotoxin, toxin

ORGANISM: Classifier
Cricetidae 86310
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
CHO cell line (cell line) [Chinese hamster ovary cell line (cell line)]
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGANISM: Classifier

Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HUVEC cell line (cell line): human umbilical vascular endothelial cells
HeLa cell line (cell line): human cervical carcinoma cells
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
L929 cell line (cell line)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species): pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
REGISTRY NUMBER: 7440-70-2 (calcium)

L115 ANSWER 25 OF 27 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:608257 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200608257
TITLE: Identification and characterization of a novel extracellular phospholipase C in Pseudomonas aeruginosa.
AUTHOR(S): Barker, A. P. [Reprint author]; Vasil, A. I. [Reprint author]; Wilderman, P. J. [Reprint author]; Filloux, A.; Vasil, M. [Reprint author]
CORPORATE SOURCE: University of Colorado Health Science Center, Denver, CO, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 289. print.
Meeting Info.: 102nd General Meeting of the American Society for Microbiology. Salt Lake City, UT, USA. May 19-23, 2002. American Society for Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002
ABSTRACT:Pseudomonas aeruginosa produces two extracellular phosphatidylcholine specific phospholipases (PC-PLC), the hemolytic PlcH and the homologous nonhemolytic PlcN. PlcH hydrolyzes phosphatidylcholine (PC) and sphingomyelin (SM), whereas PlcN hydrolyzes PC and phosphatidylserine (PS). Both have been implicated as significant virulence determinants in P. aeruginosa infections in animals and plants. Both PlcH and PlcN are

optimally expressed under phosphate (Pi) starvation. Investigation of the sec-independent twin arginine transport (TAT) secretion system, which is required for secretion of PlcH and PlcN, revealed that culture supernatants of TAT mutants still contained a Pi-starvation inducible PC-PLC and sphingomyelinase (SMase) activity. Secretion of this PC-PLC/SMase activity is dependent upon a functional Xcp machinery and it also hydrolyzes phosphatidylethanolamine in addition to PC and SM. However, its activity is not affected by the PC-PLC specific inhibitor D609 or by EDTA. Because this PC-PLC/SMase activity was only observed under Pi-starvation conditions data from Affymetrix GeneChip(R) experiments were examined for genes that were only induced under these conditions. Among these candidates, seven were selected which also encode a protein with a type II secretion signal. Insertion mutants for each of the seven candidate genes were constructed in a PA01 DELTAplcHRN background. Analysis of the Pi starvation induced culture supernatant from each of the mutants revealed that one of these mutants was entirely devoid of extracellular PC-PLC/SMase activity. This mutant contains an insertion in the P. aeruginosa gene PA0026 which encodes a protein of previously unknown function. This protein shows no significant homology to any sequence in the entire NCBI database. However this protein does contain a motif found in the zinc dependent PLCs of Bacillus cereus, Listeria monocytogenes and Clostridium perfringens. These data indicate that P. aeruginosa expresses a third novel extracellular PC-PLC and it is possible that deletion of the gene encoding this PLC would further reduce the virulence of a P. aeruginosa DELTAplcHRN mutant.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Genetics - General 03502
Genetics - Plant 03504
Genetics - Animal 03506
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Enzymes - General and comparative studies: coenzymes 10802
Bacteriology, general and systematic 30000
Physiology and biochemistry of bacteria 31000
Genetics of bacteria and viruses 31500
Medical and clinical microbiology - Bacteriology 36002
Plant physiology - Enzymes 51518
Phytopathology - Diseases caused by bacteria 54504

INDEX TERMS: Major Concepts
Bacteriology; Enzymology (Biochemistry and Molecular Biophysics); Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Diseases
Pseudomonas aeruginosa infection: bacterial disease
Pseudomonas Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals
Pseudomonas aeruginosa PlcH; Pseudomonas aeruginosa PlcN; Pseudomonas aeruginosa extracellular phosphatidylcholine-specific phospholipases; Pseudomonas aeruginosa novel extracellular phospholipase C: characterization, identification; phosphatidylcholine; phosphatidylserine; sec-independent twin arginine transport secretion system; sphingomyelin

INDEX TERMS: Miscellaneous Descriptors
inorganic phosphate starvation; Meeting Abstract

ORGANISM: Classifier
Animalia 33000

Super Taxa
Animalia
Organism Name
animal: host
Taxa Notes
Animals
ORGANISM: Classifier
Plantae 11000
Super Taxa
Plantae
Organism Name
plant: host
Taxa Notes
Plants
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa: delta-plcHRN mutant, pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
GENE NAME: Pseudomonas aeruginosa PA0026 gene (Pseudomonadaceae): insertion-dependent protein encoding

L115 ANSWER 26 OF 27 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:585038 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200585038
TITLE: Investigation of an RGD motif in the biology and biochemistry of the hemolytic phospholipase C of Pseudomonas aeruginosa.
AUTHOR(S): Stonehouse, M. J. [Reprint author]; Wadsworth, S. J.; Vasil, A. I. [Reprint author]; Vasil, M. L. [Reprint author]
CORPORATE SOURCE: Univ. of CO Health Sci. Ctr., Denver, CO, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 96. print. Meeting Info.: 102nd General Meeting of the American Society for Microbiology. Salt Lake City, UT, USA. May 19-23, 2002. American Society for Microbiology. ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2002
Last Updated on STN: 13 Nov 2002
ABSTRACT:The hemolytic phospholipase C of Pseudomonas aeruginosa is the first paradigm for a novel class of PLCs that have been identified in a number of microbial pathogens including Mycobacterium tuberculosis, Bordetella pertussis, and Burkholderia pseudomallei. The members of this class of PC-PLC do not share any amino acid homology with the well-characterized Bacillus cereus PC-PLC or similar enzymes in Clostridium perfringens and Listeria monocytogenes. The hemolytic phospholipase C is a multimeric protein composed of an enzyme (PlcH) specific for phosphatidylcholine and sphingomyelin and either one or two co-secreted chaperones (PlcR1, PlcR2) expressed from in-phase overlapping genes. In general, phospholipases (PLC) and sphingomyelinases (SMase) are capable of invoking potent signaling events in mammalian cell including those involved in cell transformation and apoptosis. Addition of

nanomolar concentrations of purified PlcHR2 onto human monocytic cells (THP1) and human umbilical vein endothelial cells (HUVEC) induces apoptosis and a release of intracellular calcium, respectively. Many PLCs and SMase have a cation requirement for activity. Both PlcH and PlcR2 bind calcium but data indicates that PlcHR2 does not require a cation for enzymatic or hemolytic activity. PlcH from P. aeruginosa along with one of the PC-PLC from B. pseudomallei are the only two members of this novel class of PLCs containing an arginine-glycine-aspartate (RGD) motif. RGD motifs are involved in integrin binding. The goal of this research is to determine the role of the RGD motif in the biology of PLC-H. This was addressed by site directed mutagenesis of the RGD motif. Wild type and mutant PLC were purified to homogeneity and their biological and biochemical properties evaluated. It has been determined that PlcHR2 binds integrin alphaIIbbeta3 and that RGD peptides blocks PlcHR2 induced calcium release in HUVECs. The data also indicate that the RGD motif plays a role in the interaction between PlcH and the chaperone proteins PlcR1,2. Additionally the data shows that along with being required for secretion, PlcR2 affects both the biological and enzymatic properties of PlcH.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - General 02502
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Enzymes - General and comparative studies: coenzymes 10802
Morphology and cytology of bacteria 30500
Physiology and biochemistry of bacteria 31000

INDEX TERMS: Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Infection

INDEX TERMS: Chemicals & Biochemicals
phosphatidylcholine; phospholipase C; sphingomyelin

INDEX TERMS: Miscellaneous Descriptors
apoptosis; Meeting Abstract

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HUVEC cell line
THP1 cell line
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa: pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER: 9001-86-9Q (phospholipase C)
63551-76-8Q (phospholipase C)

L115 ANSWER 27 OF 27 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:416578 BIOSIS Full-text

DOCUMENT NUMBER: PREV199800416578
TITLE: Pre and post-secretional interactions of hemolytic phospholipase C with a calcium-binding chaperone in ~~Pseudomonas aeruginosa~~.
AUTHOR(S): Cota-Gomez, Adela; Vasil, Michael L.; Vasil, Adriana I.
CORPORATE SOURCE: Univ. Co. Health Sci. Ctr., Denver, CO, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1998) Vol. 98, pp. 226. print.
Meeting Info.: 98th General Meeting of the American Society for Microbiology. Atlanta, Georgia, USA. May 17-21, 1998.
American Society for Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Oct 1998
Last Updated on STN: 5 Nov 1998
CONCEPT CODE: Physiology and biochemistry of bacteria 31000
Biochemistry studies - General 10060
Enzymes - General and comparative studies: coenzymes 10802
General biology - Symposia, transactions and proceedings 00520
INDEX TERMS: Major Concepts
Bacteriology; Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics)
INDEX TERMS: Chemicals & Biochemicals
calcium-binding chaperone; calmodulin; hemolytic phospholipase C; ~~sphingomyelinase~~: activity; PlcR: calcium-binding chaperone
INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
~~Pseudomonas aeruginosa~~: pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms
REGISTRY NUMBER: 9031-54-3 (~~sphingomyelinase~~)
9001-86-9 (PHOSPHOLIPASE C)

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=> d his full

     (FILE 'HOME' ENTERED AT 09:55:10 ON 14 OCT 2009)


     FILE 'ZCAPLUS' ENTERED AT 11:28:55 ON 14 OCT 2009
                D STAT QUE L74
                D IBIB ABS HITIND HITSTR L74 1-7
L92         45227 SEA SPE=ON  ABB=ON  PLU=ON  AERUGINOSA/BI
                E PSEUDOMONAS AERUGINOSA/CT
                E PSEUDOMONAS AERUGINOSA+ALL/CT
                E PSEUDOMONAS AERUGINOSA/BI OR P. AERUGINOSA/BI
L93         42657 SEA SPE=ON  ABB=ON  PLU=ON  PSEUDOMONAS AERUGINOSA/BI OR P.
                AERUGINOSA/BI
                E ACID SPHING/CT
L94             0 SEA SPE=ON  ABB=ON  PLU=ON  ACID SPHINGOMYELINASE?/CT
                E SPHINGOMYELINASE+ALL/CT
                E E2+ALL
L95          3037 SEA SPE=ON  ABB=ON  PLU=ON  SPHINGOMYELINASE?/BI
L96            30 SEA SPE=ON  ABB=ON  PLU=ON  L93 AND L95
L97          3038 SEA SPE=ON  ABB=ON  PLU=ON  ?SPHINGOMYELINAS?/BI
L98            30 SEA SPE=ON  ABB=ON  PLU=ON  L93 AND L97

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:24:57 ON 14 OCT 2009
L99            64 SEA SPE=ON  ABB=ON  PLU=ON  L98

     FILE 'ZCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:25:07 ON 14 OCT 2009
L100           45 DUP REM L98 L99 (49 DUPLICATES REMOVED)
                     ANSWERS '1-30' FROM FILE ZCAPLUS
                     ANSWERS '31-33' FROM FILE MEDLINE
                     ANSWERS '34-35' FROM FILE EMBASE
                     ANSWERS '36-45' FROM FILE BIOSIS

     FILE 'MEDLINE' ENTERED AT 12:25:57 ON 14 OCT 2009
                E P. AERU/CT
L101        40178 SEA SPE=ON  ABB=ON  PLU=ON  AERUGINOSA/BI
                D TRIAL 20-24
                D TRIAL 200-205

     FILE 'ZCAPLUS' ENTERED AT 12:44:41 ON 14 OCT 2009

     FILE 'REGISTRY' ENTERED AT 12:45:41 ON 14 OCT 2009
L102            1 SEA SPE=ON  ABB=ON  PLU=ON  9031-54-3
                D SCA
                E ACID SPHINGOMYELINASE/CN
L103            1 SEA SPE=ON  ABB=ON  PLU=ON  ACID SPHINGOMYELINASE/CN

     FILE 'ZCAPLUS' ENTERED AT 12:46:32 ON 14 OCT 2009
L104         2159 SEA SPE=ON  ABB=ON  PLU=ON  L103
                E ACID SPHINGOMYELINAS?/BI
L105          624 SEA SPE=ON  ABB=ON  PLU=ON  ACID SPHINGOMYELINAS?/BI
L106           11 SEA SPE=ON  ABB=ON  PLU=ON  L93 AND L105
L107           19 SEA SPE=ON  ABB=ON  PLU=ON  L98 NOT L106
L108           24 SEA SPE=ON  ABB=ON  PLU=ON  L103 AND L93
L109           30 SEA SPE=ON  ABB=ON  PLU=ON  L98 OR L108

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:49:44 ON 14 OCT 2009
L110         1623 SEA SPE=ON  ABB=ON  PLU=ON  ACID SPHINGOMYELINAS?/BI
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L111         30 SEA SPE=ON  ABB=ON  PLU=ON  L93 AND L110
                D TRIAL 1-5

     FILE 'REGISTRY' ENTERED AT 12:51:27 ON 14 OCT 2009

     FILE 'ZCAPLUS' ENTERED AT 12:51:36 ON 14 OCT 2009
                D STAT QUE L106

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:51:47 ON 14 OCT 2009
                D STAT QUE L111

     FILE 'ZCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:51:59 ON 14 OCT 2009
L112         18 DUP REM L106 L111 (23 DUPLICATES REMOVED)
                       ANSWERS '1-11' FROM FILE ZCAPLUS
                       ANSWERS '12-13' FROM FILE MEDLINE
                       ANSWER '14' FROM FILE EMBASE
                       ANSWERS '15-18' FROM FILE BIOSIS
                D IALL HITSTR L112 1-11
                D IALL L112 12-18

     FILE 'REGISTRY' ENTERED AT 12:53:18 ON 14 OCT 2009

     FILE 'ZCAPLUS' ENTERED AT 12:53:22 ON 14 OCT 2009
                D STAT QUE L109
L113         19 SEA SPE=ON  ABB=ON  PLU=ON  L109 NOT L106

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:53:52 ON 14 OCT 2009
                D STAT QUE L99
L114         34 SEA SPE=ON  ABB=ON  PLU=ON  L99 NOT L111

     FILE 'ZCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 12:54:10 ON 14 OCT 2009
L115         27 DUP REM L113 L114 (26 DUPLICATES REMOVED)
                       ANSWERS '1-19' FROM FILE ZCAPLUS
                       ANSWER '20' FROM FILE MEDLINE
                       ANSWER '21' FROM FILE EMBASE
                       ANSWERS '22-27' FROM FILE BIOSIS
                D IALL HITSTR L115 1-19
                D IALL L115 20-27


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   12 OCT 2009  HIGHEST RN 1187916-70-6
     DICTIONARY FILE UPDATES:  12 OCT 2009  HIGHEST RN 1187916-70-6

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:
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http://www.cas.org/support/stngen/stndoc/properties.html

FILE ZCAPLUS

FILE COVERS 1907 - 14 Oct 2009 VOL 151 ISS 16
FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

ZCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 13 Oct 2009 (20091013/UP). FILE COVERS 1949 TO DATE.

MEDLINE and LMEDLINE have been updated with the 2009 Medical Subject Headings (MeSH) vocabulary and tree numbers from the U.S. National Libra of Medicine (NLM). Additional information is available at

http://www.nlm.nih.gov/pubs/techbull/nd08/nd08_medline_data_changes_2009.

On February 21, 2009, MEDLINE was reloaded. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

FILE EMBASE
FILE COVERS 1974 TO 14 Oct 2009 (20091014/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE

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      codes.

      For further assistance, please contact your local helpdesk.

     FILE BIOSIS
     FILE COVERS 1926 TO DATE.
     CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
     FROM JANUARY 1926 TO DATE.

     RECORDS LAST ADDED: 7 October 2009 (20091007/ED)

     BIOSIS has been augmented with 1.8 million archival records from 1926
     through 1968.  These records have been re-indexed to match current
     BIOSIS indexing.

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